(predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295, TANGO 354, or TANGO 378 protein and/or nucleic acid expression as well as INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295, TANGO 354, or TANGO 378 activity, in the context of a biological sample (e.g., blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant or unwanted INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295, TANGO 354, or TANGO 378 gene expression or activity. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295, TANGO 354, or TANGO 378 protein or nucleic acid expression or activity. For example, mutations in a gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with protein or nucleic acid expression or activity.

As an alternative to making determinations based on the absolute expression level of selected genes, determinations may be based on the normalized expression levels of these genes. Expression levels are normalized by correcting the absolute expression level of a INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295, TANGO 354, or TANGO 378 gene by comparing its expression to the expression of a gene that is not a INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295, TANGO 354, or TANGO 378, e.g., a housekeeping gene that is constitutively expressed. Suitable genes for normalization include housekeeping genes such as the actin gene. This normalization allows the comparison of the expression level in one sample, e.g., a patient sample, to another sample, e.g., a non-disease sample, or between samples from different sources.

Alternatively, the expression level can be provided as a relative expression level. To determine a relative expression level of a gene, the level of expression of the gene is determined for 10 or more samples of different cell isolates, preferably 50 or more samples, prior to the determination of the expression level for the sample in question. The mean expression level of each of the genes assayed in the larger number of samples is determined and this is used as a baseline expression level for the gene(s) in question. The expression level of the gene determined for the test sample (absolute level of expression) is then divided by the mean expression value obtained for that gene. This provides a relative expression level and aids in identifying extreme cases of disease.

Preferably, the samples used in the baseline determination will be from diseased or from non-diseased cells of tissue. The choice of the cell source is dependent on the use of

- 102 -

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the relative expression level. Using expression found in normal tissues as a mean expression score aids in validating whether the INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295, TANGO 354, or TANGO 378 gene assayed is diseased cell-type specific (versus normal cells). Such a use is particularly important in identifying whether a INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295,

TANGO 354, or TANGO 378 gene can serve as a target gene. In addition, as more data is accumulated, the mean expression value can be revised, providing improved relative expression values based on accumulated data. Expression data from cells provide a means for grading the severity of the disease state.

Another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of INTERCEPT 340, MANGO 003, MANGO 347, TANGO 272, TANGO 295, TANGO 354, or TANGO 378 genes in clinical trials.

These and other agents are described in further detail in the following sections.

### 15 1. <u>Diagnostic Assays</u>

An exemplary method for detecting the presence or absence of a polypeptide or nucleic acid of the invention in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting a polypeptide or nucleic acid (e.g., mRNA, genomic DNA) of the invention such that the presence of a polypeptide or nucleic acid of the invention is detected in the biological sample. A preferred agent for detecting mRNA or genomic DNA encoding a polypeptide of the invention is a labeled nucleic acid probe capable of hybridizing to mRNA or genomic DNA encoding a polypeptide of the invention. The nucleic acid probe can be, for example, a full-length cDNA, such as the nucleic acid of SEQ ID NOs:1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28 or 30, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to a mRNA or genomic DNA encoding a polypeptide of the invention. Other suitable probes for use in the diagnostic assays of the invention are described herein.

A preferred agent for detecting a polypeptide of the invention is an antibody capable of binding to a polypeptide of the invention, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')<sub>2</sub>) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly

labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect mRNA, protein, or genomic DNA in a biological sample in vitro as well as in vivo. For example, in vitro techniques for detection of mRNA include Northern hybridizations and in situ hybridizations. In vitro techniques for detection of a polypeptide of the invention include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. In vitro techniques for detection of genomic DNA include Southern hybridizations. Furthermore, in vivo techniques for detection of a polypeptide of the invention include introducing into a subject a labeled antibody directed against the polypeptide. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting a polypeptide of the invention or mRNA or genomic DNA encoding a polypeptide of the invention, such that the presence of the polypeptide or mRNA or genomic DNA encoding the polypeptide is detected in the biological sample, and comparing the presence of the polypeptide or mRNA or genomic DNA encoding the polypeptide in the control sample with the presence of the polypeptide or mRNA or genomic DNA encoding the polypeptide in the test sample.

The invention also encompasses kits for detecting the presence of a polypeptide or nucleic acid of the invention in a biological sample (a test sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing a disorder associated with aberrant expression of a polypeptide of the invention (e.g., a proliferative disorder, e.g., psoriasis or cancer). For example, the kit can comprise a labeled compound or agent capable of detecting the polypeptide or mRNA encoding the polypeptide in a biological sample and means for determining the amount of the polypeptide or mRNA in the sample (e.g., an antibody which binds the polypeptide or an oligonucleotide probe which binds to DNA or mRNA encoding the polypeptide). Kits can also include instructions for observing that the tested subject is suffering from or is at risk of developing

- 104 -

a disorder associated with aberrant expression of the polypeptide if the amount of the polypeptide or mRNA encoding the polypeptide is above or below a normal level.

For antibody-based kits, the kit can comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to a polypeptide of the invention; and, optionally, (2) a second, different antibody which binds to either the polypeptide or the first antibody and is conjugated to a detectable agent.

For oligonucleotide-based kits, the kit can comprise, for example: (1) an oligonucleotide, e.g., a detectably labeled oligonucleotide, which hybridizes to a nucleic acid sequence encoding a polypeptide of the invention or (2) a pair of primers useful for amplifying a nucleic acid molecule encoding a polypeptide of the invention. The kit can also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent. The kit can also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit can also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for observing whether the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of the polypeptide.

#### 2. Prognostic Assays

5

The methods described herein can furthermore be utilized as diagnostic or prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with aberrant expression or activity of a polypeptide of the invention. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or at risk of developing a disorder associated with aberrant expression or activity of a polypeptide of the invention. Alternatively, the prognostic assays can be utilized to identify a subject having or at risk for developing such a disease or disorder. Thus, the present invention provides a method in which a test sample is obtained from a subject and a polypeptide or nucleic acid (e.g., mRNA, genomic DNA) of the invention is detected, wherein the presence of the polypeptide or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant expression or activity of the polypeptide. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (e.g., serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to

treat a disease or disorder associated with aberrant expression or activity of a polypeptide of the invention. For example, such methods can be used to determine whether a subject can be effectively treated with a specific agent or class of agents (e.g., agents of a type which decrease activity of the polypeptide). Thus, the present invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant expression or activity of a polypeptide of the invention in which a test sample is obtained and the polypeptide or nucleic acid encoding the polypeptide is detected (e.g., wherein the presence of the polypeptide or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant expression or activity of the polypeptide).

The methods of the invention can also be used to detect genetic lesions or mutations in a gene of the invention, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized aberrant expression or activity of a polypeptide of the invention. In preferred embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion or mutation characterized by at least one of an alteration affecting the integrity of a gene encoding the polypeptide of the invention, or the mis-expression of the gene encoding the polypeptide of the invention. For example, such genetic lesions or mutations can be detected by ascertaining the existence of at least one of: 1) a deletion of one or more nucleotides from the gene; 2) an addition of one or more nucleotides to the gene; 3) a substitution of one or more nucleotides of the gene; 4) a chromosomal rearrangement of the gene; 5) an alteration in the level of a messenger RNA transcript of the gene; 6) an aberrant modification of the gene, such as of the methylation pattern of the genomic DNA; 7) the presence of a non-wild type splicing pattern of a messenger RNA transcript of the gene; 8) a non-wild type level of a the protein encoded by the gene; 9) an allelic loss of the gene; and 10) an inappropriate post-translational modification of the protein encoded by the gene. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions in a gene.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (see, e.g., U.S. Patent NOs. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (see, e.g., Landegran et al., 1988, Science 241:1077-80; and Nakazawa et al., 1994, Proc. Natl. Acad. Sci. USA 91:360-4), the latter of which can be particularly useful for detecting point mutations in a gene (see, e.g., Abravaya et al., 1995, Nucleic Acids Res. 23:675-82). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (e.g., genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to the selected

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10

gene under conditions such that hybridization and amplification of the gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (Guatelli et al., 1990, *Proc. Natl. Acad. Sci. USA* 87:1874-78), transcriptional amplification system (Kwoh, et al., 1989, *Proc. Natl. Acad. Sci. USA* 86:1173-7), Q-Beta Replicase (Lizardi et al., 1988, *Bio/Technology* 6:1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in a selected gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (see, e.g., U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations can be identified by hybridizing a sample and control nucleic acids, e.g., DNA or RNA, to high density arrays containing hundreds or thousands of oligonucleotides probes (Cronin et al., 1996, Human Mutation 7:244-55; Kozal et al., 1996, Nature Medicine 2:753-9). For example, genetic mutations can be identified in two-dimensional arrays containing light-generated DNA probes as described in Cronin et al., supra. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This step is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the selected gene and detect mutations by comparing the sequence of the sample nucleic acids with the corresponding wild-type (control)

sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert (1977, *Proc. Natl. Acad. Sci. USA* 74:560) or Sanger (1977, *Proc. Natl. Acad. Sci. USA* 74:5463). It is also contemplated that any of a variety of automated sequencing procedures can be utilized when performing the diagnostic assays developed by Naeve et al. (1995, *Bio/Techniques* 19:448-53), including sequencing by mass spectrometry (*see*, *e.g.*, PCT Publication No. WO 94/16101; Cohen et al., 1996, *Adv. Chromatogr.* 36:127-62; and Griffin et al., 1993, *Appl. Biochem. Biotechnol.* 38:147-59).

Other methods for detecting mutations in a selected gene include methods in which protection from cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes (Myers et al., 1985, *Science* 230:1242). In general, the technique of mismatch cleavage entails providing heteroduplexes formed by hybridizing (labeled) RNA or DNA containing the wild-type sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent which cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and sample strands. RNA/DNA duplexes can be treated with RNase to digest mismatched regions, and DNA/DNA hybrids can be treated with S1 nuclease to digest mismatched regions.

In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton et al., 1988, Proc. Natl. Acad. Sci. USA 85:4397; Saleeba et al., 1992, Methods Enzymol. 217:286-95. In a preferred embodiment, the control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize mismatched base pairs in double-stranded DNA (so called DNA mismatch repair enzymes) in defined systems for detecting and mapping point mutations in cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches (Hsu et al., 1994, *Carcinogenesis* 15:1657-62). According to an exemplary embodiment, a probe based on a selected sequence, *e.g.*, a wild-type sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. *See, e.g.*, U.S. Patent No. 5,459,039.

In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type

nucleic acids (Orita et al., 1989, *Proc. Natl. Acad. Sci. USA* 86:2766; *see also* Cotton, 1993, *Mutat. Res.* 285:125-44; Hayashi, 1992, *Genet. Anal. Tech. Appl.* 9:73-9). Single-stranded DNA fragments of sample and control nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, and the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In a preferred embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in electrophoretic mobility (Keen et al., 1991, *Trends Genet.* 7:5).

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE) (Myers et al., 1985, *Nature* 313:495). When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a 'GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA (Rosenbaum and Reissner, 1987, *Biophys. Chem.* 265:12753).

Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions which permit hybridization only if a perfect match is found (Saiki et al., 1986, *Nature* 324:163; Saiki et al., 1989, *Proc. Natl. Acad. Sci. USA* 86:6230). Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification technology which depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization; Gibbs et al., 1989, *Nucleic Acids Res.* 17:2437-48) or at the extreme 3' end of one primer where, under appropriate conditions, mismatch can prevent or reduce polymerase extension (Prossner, 1993, *Tibtech* 11:238). In addition, it may be desirable to introduce a novel restriction site in the region of the mutation to create cleavage-based detection (Gasparini et al., 1992, *Mol. Cell Probes* 6:1). It is anticipated that in certain embodiments amplification may also be

performed using Taq ligase for amplification (Barany, 1991, *Proc. Natl. Acad. Sci. USA* 88:189). In such cases, ligation will occur only if there is a perfect match at the 3' end of the 5' sequence making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of amplification.

The methods described herein may be performed, for example, by utilizing prepackaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used, e.g., in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving a gene encoding a polypeptide of the invention. Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which the polypeptide of the invention is expressed may be utilized in the prognostic assays described herein.

#### 3. Pharmacogenomics

Agents, or modulators which have a stimulatory or inhibitory effect on activity or expression of a polypeptide of the invention as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders associated with aberrant activity of the polypeptide. In conjunction with such treatment, the pharmacogenomics (i.e., the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of a polypeptide of the invention, expression of a nucleic acid of the invention, or mutation content of a gene of the invention in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Linder, 1997, Clin. Chem. 43(2):254-66. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase deficiency (G6PD) is a common inherited enzymopathy in which the main

clinical complication is haemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (e.g., N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, a PM will show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of a polypeptide of the invention, expression of a nucleic acid encoding the polypeptide, or mutation content of a gene encoding the polypeptide in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a modulator of activity or expression of the polypeptide, such as a modulator identified by one of the exemplary screening assays described herein.

## 30 4. Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of a polypeptide of the invention (e.g., the ability to modulate aberrant cell proliferation chemotaxis, and/or differentiation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent, as determined by a screening assay as described herein, to increase gene expression, protein levels or protein activity, can be monitored in clinical trials of subjects exhibiting decreased

gene expression, protein levels, or protein activity. Alternatively, the effectiveness of an agent, as determined by a screening assay, to decrease gene expression, protein levels or protein activity, can be monitored in clinical trials of subjects exhibiting increased gene expression, protein levels, or protein activity. In such clinical trials, expression or activity of a polypeptide of the invention and preferably, that of other polypeptide that have been implicated in for example, a cellular proliferation disorder, can be used as a marker of the immune responsiveness of a particular cell.

For example, and not by way of limitation, genes, including those of the invention, that are modulated in cells by treatment with an agent (e.g., compound, drug or small molecule) which modulates activity or expression of a polypeptide of the invention (e.g., as identified in a screening assay described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of expression of a gene of the invention and other genes implicated in the disorder. The levels of gene expression (i.e., a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of a gene of the invention or other genes. In this way, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of the polypeptide or nucleic acid of the invention in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level the of the polypeptide or nucleic acid of the invention in the post-administration samples; (v) comparing the level of the polypeptide or nucleic acid of the invention in the pre-administration sample with the level of the polypeptide or nucleic acid of the invention in the post-administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of the polypeptide to higher levels than detected, i.e., to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of the polypeptide to lower levels than detected, i.e., to decrease the effectiveness of the agent.

#### C. Methods of Treatment

The present invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant expression or activity of a polypeptide of the invention, e.g., cardiac infection (e.g., myocarditis or dilated cardiomyopathy), central nervous system infection (e.g., non-specific febrile illness or meningoencephalitis), pancreatic infection (e.g., acute pancreatitis), respiratory infection (pneumonia), gastrointestinal infection, type I diabetes, cancer, familia hypercholesterolemia, treat hemophilia B, Marfan syndrome, protein S deficiency, allergy, inflammation, and gastroduodenal ulcer. Moreover, the polypeptides of the invention can be used to modulate cellular function, survival, morphology, proliferation and/or differentiation.

#### 1. Prophylactic Methods

In one aspect, the invention provides a method for preventing in a subject, a disease or condition associated with an aberrant expression or activity of a polypeptide of the invention, by administering to the subject an agent which modulates expression or at least one activity of the polypeptide. Subjects at risk for a disease which is caused or contributed to by aberrant expression or activity of a polypeptide of the invention can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the aberrancy, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending on the type of aberrancy, for example, an agonist or antagonist agent can be used for treating the subject.

#### 2. Therapeutic Methods

Another aspect of the invention pertains to methods of modulating expression or activity of a polypeptide of the invention for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of the polypeptide. An agent that modulates activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of the polypeptide, a peptide, a peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more of the biological activities of the polypeptide. Examples of such stimulatory agents include the active polypeptide of the invention and a nucleic acid molecule encoding the polypeptide of the invention that has been introduced into the cell. In another embodiment, the agent inhibits one or more of the biological activities of the polypeptide of the invention. Examples of such inhibitory agents include antisense nucleic acid molecules and antibodies. These modulatory methods can be performed in vitro (e.g.,

by culturing the cell with the agent) or, alternatively, in vivo (e.g., by administering the agent to a subject). As such, the present invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of a polypeptide of the invention. In one embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that modulates (e.g., upregulates or downregulates) expression or activity. In another embodiment, the method involves administering a polypeptide of the invention or a nucleic acid molecule of the invention as therapy to compensate for reduced or aberrant expression or activity of the polypeptide.

Stimulation of activity is desirable in situations in which activity or expression is abnormally low or downregulated and/or in which increased activity is likely to have a beneficial effect. Conversely, inhibition of activity is desirable in situations in which activity or expression is abnormally high or upregulated and/or in which decreased activity is likely to have a beneficial effect.

The contents of all references, patents and published patent applications cited throughout this application are hereby incorporated by reference.

#### Deposit of Clones

Clones containing cDNA molecules encoding human MANGO 003 were deposited with the American Type Culture Collection (ATCC® 10801 University Boulevard, Manassas, VA 20110-2209) on March 30, 1999 as Accession Number 207178, as part of a composite deposit representing a mixture of three strains, each carrying one recombinant plasmid harboring a particular cDNA clone.

To distinguish the strains and isolate a strain harboring a particular cDNA clone, an aliquot of the mixture can be streaked out to single colonies on nutrient medium (e.g., LB plates) supplemented with 100 g/ml ampicillin, single colonies grown, and then plasmid DNA extracted using a standard minipreparation procedure. Next, a sample of the DNA minipreparation can be digested with a combination of the restriction enzymes Sal I and Not I, and the resultant products resolved on a 0.8% agarose gel using standard DNA electrophoresis conditions. The digest liberates fragments as follows:

human MANGO 003 (clone EpthLa6a1): 3.2 kB

The identity of the strains can be inferred from the fragments liberated.

Clones containing cDNA molecules encoding human INTERCEPT 340, MANGO 347, and TANGO 272 were deposited with the American Type Culture Collection (ATCC®)

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10801 University Boulevard, Manassas, VA 20110-2209) on June 18, 1999 as Accession Number PTA-250, as part of a composite deposit representing a mixture of three strains, each carrying one recombinant plasmid harboring a particular cDNA clone.

To distinguish the strains and isolate a strain harboring a particular cDNA clone, an aliquot of the mixture can be streaked out to single colonies on nutrient medium (e.g., LB plates) supplemented with 100 g/ml ampicillin, single colonies grown, and then plasmid DNA extracted using a standard minipreparation procedure. Next, a sample of the DNA minipreparation can be digested with a combination of the restriction enzymes Sal I and Not I, and the resultant products resolved on a 0.8% agarose gel using standard DNA electrophoresis conditions. The digest liberates fragments as follows:

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human INTERCEPT 340 (clone EpI340): 3.3 kB human MANGO 347 (clone EpM347): 1.4 kB human TANGO 272 (clone EpT272): 5.0 kB

The identity of the strains can be inferred from the fragments liberated.

Clones containing cDNA molecules encoding human TANGO 295, TANGO 354, and TANGO 378 were deposited with the American Type Culture Collection (ATCC® 10801 University Boulevard, Manassas, VA 20110-2209) on June 18, 1999 as Accession Number PTA-249, as part of a composite deposit representing a mixture of three strains, each carrying one recombinant plasmid harboring a particular cDNA clone.

To distinguish the strains and isolate a strain harboring a particular cDNA clone, an aliquot of the mixture can be streaked out to single colonies on nutrient medium (e.g., LB plates) supplemented with 100 g/ml ampicillin, single colonies grown, and then plasmid

DNA extracted using a standard minipreparation procedure. Next, a sample of the DNA minipreparation can be digested with a combination of the restriction enzymes Sal I and Not I, and the resultant products resolved on a 0.8% agarose gel using standard DNA electrophoresis conditions. The digest liberates fragments as follows:

human TANGO 295 (clone EpT295): 1.5 kB
 human TANGO 354 (clone EpT354): 1.8 kB
 human TANGO 378 (clone EpT378): 3.3 kB

The identity of the strains can be inferred from the fragments liberated.

All publications, patents and patent applications mentioned in this specification are herein incorporated by reference into the specification to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference.

## 5 Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following Claims.

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International Application No: PCT/

MICROORGANISMS
Optional Sheet in connection with the microorganism referred to on pages, lines of the description '
A. IDENTIFICATION OF DEPOSIT <sup>2</sup>
Further deposits are identified on an additional sheet '
Name of depositary institution '
American Type Culture Collection
· · · · · · · · · · · · · · · · · · ·
Address of depositary institution (including postal code and country) *
10801 University Bivd.
Manassas, VA 20110-2209 US
Date of deposit * March 30, 1999 Accession Number * 207178
B. ADDITIONAL INDICATIONS ' (leave blank if not applicable). This information is continued on a separate attached sheet
•
C. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (If the Indications are pot all designated States)
D. SEPARATE FURNISHING OF INDICATIONS ' (leave blank if not applicable)
The Indications listed below will be submitted to the International Bureau later ' (Specify the general nature of the Indications e.g., "Accession Number of Deposit")
E. This sheet was received with the International application when filed (to be checked by the receiving Office)
1 10
sugtta loure
(Authorized Officer)
☐ The date of receipt (from the applicant) by the International Bureau *
was
(Authorized Officer)
Form PCT/RO/134 (January 1981)

International Application No: PCT/

Form PCT/RO/134 (cont.)

American Type Culture Collection

10801 University Blvd. Manassas, VA 20110-2209 US

Accession No.	Date of Deposit							
PTA-249	June 18, 1999							
PTA-250	June 18, 1999							

#### What is claimed is:

- 1. An isolated nucleic acid molecule selected from the group consisting of:
- a) a nucleic acid molecule comprising a nucleotide sequence which is at least 55% identical to the nucleotide sequence of SEQ ID NOs:1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250, or a complement thereof;
- b) a nucleic acid molecule comprising a fragment of at least 300 nucleotides of the nucleotide sequence of SEQ ID NOs:1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250, or a complement thereof;
- c) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250;
  - d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250; and
- a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20,

23, 26, 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NOs:1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, or a complement thereof, under stringent conditions.

- 2. The isolated nucleic acid molecule of Claim 1, which is selected from the group consisting of:
- a) a nucleic acid comprising the nucleotide sequence of SEQ ID NOs:1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250, or a complement thereof; and
- b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250.
- 3. The nucleic acid molecule of Claim 1 further comprising vector nucleic acid sequences.
  - 4. The nucleic acid molecule of Claim 1 further comprising nucleic acid sequences encoding a heterologous polypeptide.
    - 5. A host cell which contains the nucleic acid molecule of Claim 1.
    - 6. The host cell of Claim 5 which is a mammalian host cell.
- 7. A non-human mammalian host cell containing the nucleic acid molecule of Claim 1.
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  - 8. An isolated polypeptide selected from the group consisting of:

- 118 -

- a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, or 29, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, or 29;
- a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, or 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250, wherein the polypeptide is encoded by a nucleic acid molecule which 10 hybridizes to a nucleic acid molecule comprising SEQ ID NOs: 1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, or a complement thereof under stringent conditions; and
- a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 55% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NOs:1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, or a complement thereof.
  - 9. The isolated polypeptide of Claim 8 comprising the amino acid sequence of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, or 29.
- The polypeptide of Claim 8 further comprising heterologous amino acid 10. 20 sequences.
  - 11. An antibody which selectively binds to a polypeptide of Claim 8.
- 12. A method for producing a polypeptide selected from the group consisting of: 25 a) a polypeptide comprising the amino acid sequence of SEQ ID NOs:2, 5, 8,
- 11, 14, 17, 20, 23, 26, or 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250;
  - a polypeptide comprising a fragment of the amino acid sequence of SEQ ID b) NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, or 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as
- Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250, wherein the

fragment comprises at least 15 contiguous amino acids of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, or 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250; and

c) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NOs:2, 5, 8, 11, 14, 17, 20, 23, 26, or 29, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number 207178, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-249, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC® as Accession Number PTA-250, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule comprising SEQ ID NOs:1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, or a complement thereof under stringent conditions:

comprising culturing the host cell of Claim 5 under conditions in which the nucleic acid molecule is expressed.

- 13. A method for detecting the presence of a polypeptide of Claim 8 in a sample, comprising:
  - a) contacting the sample with a compound which selectively binds to a polypeptide of Claim 8; and
    - b) determining whether the compound binds to the polypeptide in the sample.
- 25 14. The method of Claim 13, wherein the compound which binds to the polypeptide is an antibody.
  - 15. A kit comprising a compound which selectively binds to a polypeptide of Claim 8 and instructions for use.
  - 16. A method for detecting the presence of a nucleic acid molecule of Claim 1 in a sample, comprising the steps of:
  - a) contacting the sample with a nucleic acid probe or primer which selectively hybridizes to the nucleic acid molecule; and
- b) determining whether the nucleic acid probe or primer binds to a nucleic acid molecule in the sample.

- 120 -

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- 17. The method of Claim 16, wherein the sample comprises mRNA molecules and is contacted with a nucleic acid probe.
- 18. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of Claim 1 and instructions for use.
- 19. A method for identifying a compound which binds to a polypeptide of Claim 8 comprising the steps of:
- a) contacting a polypeptide, or a cell expressing a polypeptide of Claim 8 with a test compound; and
  - b) determining whether the polypeptide binds to the test compound.
- 20. The method of Claim 19, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:
- a) detection of binding by direct detecting of test compound/polypeptide binding;
  - b) detection of binding using a competition binding assay;
  - c) detection of binding using an assay for INTERCEPT 340-, MANGO 003-, MANGO 347-, TANGO 272-, TANGO 295-, TANGO 354-, or TANGO 378-mediated signal transduction.
  - 21. A method for modulating the activity of a polypeptide of Claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of Claim 8 with a compound which binds to the polypeptide in a sufficient concentration to modulate the activity of the polypeptide.
  - 22. A method for identifying a compound which modulates the activity of a polypeptide of Claim 8, comprising:
    - a) contacting a polypeptide of Claim 8 with a test compound; and
- b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

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Input file I340Athsa102b12; Output File I340Athsa102b12.pat Sequence length 3284

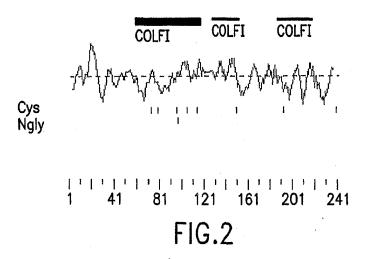
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CATTACCTAAATTTTACCATTAACATTTTACCCTGCTGGCATTATTGTGCTTATCCATCTACGTATCCCTCTCCCTT	237
CATTGGTGTATTTCTAAGTAAATTGTAGGCCTCAGTACACTTCCTTC	316
TCCATTTTTAAAAGAGCAATTCTTGATAGATTTATATAGTTTTGTAAAATGTTCATATAGAGCTACAAATTTTATCTTT	395
TTGTTTCTTATTGTATGTCTAGGGTCCTGAAGGGGATGCTGGCATTGTTGGGATATCAGGTCCTAAAGGTCCTATTGGA	474
CACAGAGGAAACACTGGTCCCCTTGGCAGAGAAGGTATAATAGGCCCCAACAGGTAGAACTGGACCCAGAGGTGAAAAGG	553
GCTTTAGAGGTGAAACTGGTCCTCAAGGACCAAGAGGTCAACCAGGGCCTCCAGGTCCACCTGGAGCACCAGGCCCAAG	632
AAAGCAAATGGATATCAATGCTGCTATTCAAGCCTTGATTGA	711
GTTTTATTTATATTGGCACTGTCTCTCAATATACCAATTAAACAGAGAAAATTTTTGGAGGCCAAAATGTGACATTATC	790
TCAAAGATTGTATTTAAAACAGATTGAAAATGTGAAAACCATTCTCAAGAACAAAGTAAGT	869
AGAAATATATGCGTAGGATGTTTTGTAAGGAAAACATTTAAATCAAAAATTTAGTACTGTTATTTGTAAGGAATTTGGT	948
ACTATCCAAGAAAGTAGTTAAATGAGGTTAGCCATGTTTCTTAAAATGAGATATATAT	1027
AAACTCTAATGATTCAATGTGTAATTTAAAAAACATAATACAGTAGACATAGCAATTCTTATGTTAGCTTGAAAACTAA	1106
ACTTGCAAATGTGAATTTAACCTCTTTAAAAGATTAAGGTTATTAAAGCATACACATATGCCTATGCTTAAATATAAAC	1185
M E T H S S P A L A TGTTCTTTACATTCTACTCACAACTTACTACACATA ATG GAA ACA CAT TCT TCT CCT GCC TTG GCC 1	10 251
H V G P Q D F F V Y I I L M M T W Q S Y CAT GTT GGT CCT CAG GAT TIT TIT GTT TAT ATA ATT CTT ATG ATG ACT TGG CAG AGC TAC	30 1311
Q N T E V T L I D H S E E I F K T L N Y CAG AAT ACT GAA GTG ACT TTA ATT GAC CAC AGT GAA GAG ATA TTC AAA ACC CTG AAC TAC	50 1371

FIG.1A

										-, -	_									
																			R CGA	70 1431
			D GAT																D GAC	90 1491
			G GGC																G GGC	110 1551
			L TTA																Q CAG	130 1611
			L CTT																L CTA	150 1671
			R AGG																	170 1731
			G GGC																	190 1791
			I ATT																E GAA	210 1851
			L CTT																	230 1911
			D GAC															•		242 1947
			AGTT																	2026
			CATO																	2105
AAAA	GGCA	TTTT	TAAA	AGGAC	TATO	SATTO	ATAA	AGTA	ATTTA	AATTO	TTT	AAAA	ATTA	TATI	CATC	TCAG	CTTI	CŤTA	AGAG	2184
AATT	CCCT	AGAA	CTAA	TAAA	TATT	TAAAT	ATGG	TTAA	CTTC	CAGGG	TATO	TTAT	ATTT	TTGA	CTGA	GTGC	GTAG	STACC	CAT	2263
TAGA	CAGC	TGGA	GATG	CAGA	GCAC	TATG	GAGC	AATA	CTGG	CTAA	TGCT	TCCA	GATG	TGCA	CTGC	TTCT	GTCT	AAAA	ATT	2342
ACAA	GCCA	CAGT	CTAA	TATG	TCTT	ATTT	TCCA	AAAC	ACTA	AGCT	GTAT	TCAG	GTCC	CCGA	TGGG	CATA	TACA	TCTT	AGC	2421

CGGTGATACACTACCTCTTACGTGTTGCCTCTTTGTGTTGCTTGGTGCTCTTTCGAAAACAAGGTGCTTATGGCTTTCA	2500
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CAAATTTTTTGAAATTGCTGCTGTTTTAAATTATAAAACCTTTATATTTCTGCTTTGTAGAAATTATATGTTTTGTAGT	2974
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GTTCAATACTGAAAGAAAAATATTATACCTCTTGGTATCTAGAAAAGCTTGTTCATCCATTATAAATATATCTTTAGCC	3211
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FIG.1C



COLFI: domain 1 of 3, from 58 to 116: score 110.3, E = 1.3e-42

\*->IksPeGksrknPARtCkDLfLchpefksGeYWiDPNqGCikDAikVf +k+P+G +r+nPAR CkDL c + ++G YWiDPN+GC+ DAi+Vf INT340 58 IKNPLG-TRDNPARICKDLLNCEQKVSDGKYWIDPNLGCPSDAIEVF 103

CnkrfetGvgeTCisp<-\*
Cn f +G g+TC +p
INT340 104 CN-FSAG-GQTCLPP 116

COLFI: domain 2 of 3, from 126 to 151: score 9.7, E = 0.0028

\*->isnvQ1TFLRLLSteAsQNiTYhCKN<-\*
+++vQ+ FL LLS+eA iT hC N
INT340 126 VGKVQMNFLHLLSSEATHIITIHCLN 151

COLFI: domain 3 of 3, from 186 to 217: score 5.8, E = 0.09

\*->tvIGeDGCssrtgewgKTViEyeTkKttRLPIv<-\*
+vl D C+ g w K+ + + T+ + +LP +

1NT340 186 KVL-SDDCKIQDGSWHKATFLFHTQEPNQLPV1 217

FIG.3

6/95
Input file M003Athyo30d3; Output File M003AthYo30d3.pot Sequence length 3169

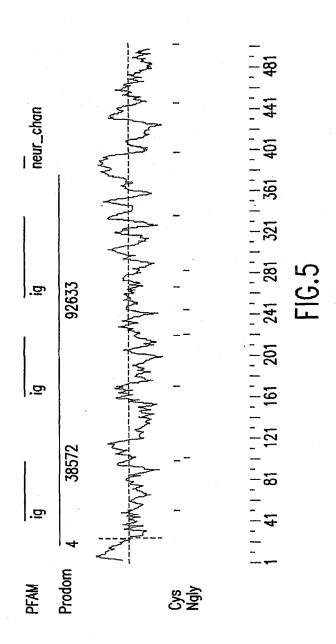
GTC	M T P S P TCGACCCACGCGTCCGCCGCCGAGGTCCGGACAGGCCGAG ATG ACG CCG AGC CCC															5 71				
						P CCG														25 131
R CGA						A GCG							-						R CGC	45 191
T ACT	V GTG		L CTG	-		P CCA										M ATG		T ACC		65 251
						S AGC														85 311
						E GAG														105 371
. G GGC						Y TAC														125 431
						S TCC											Q CAG	W TGG	A GCA	145 491
						P														165 551
S AGC						C TGC												W TGG	M ATG	185 611
K AAG	D GAC	D GAC				T ACG								R AGG		K AAG		W TGG	T ACA	205 671
L CTG						R CGG											V GTG		N AAC	225 731
R CGC						A GCC											R CGT	S TCC		245 791

FIG.4A SUBSTITUTE SHEET (RULE 26)

											1/2	, <u>u</u>									
																				S TCC	265 851
-																		R CGC			285 911
																		F TTT			<b>3</b> 05 971
					D GAC												K AAG	L CTG	L CTC	I	325 1031
																		T			345 1091
																		G GGG			365 1151
																		I ATC			385 1211
																		K AAG			405 1271
																		A GCC			425 1331
																		G GGT			445 1391
	L CTG				H Cat		,											G GGC			465 1451
	A GCT																	H CAC			485 1511
					S TCA											H CAC	Y TAT	Q CAG	C TGC	* TAG	505 1571
	ACGG	CACC	GTAT	CTGC	CAGTO	GGCA	CGGG	GGGG	CCGG	CCAC	ACAG	GCAG	ACTO	GGAG	GATO	GAGG	ACGG	AGCT	GCAG	ACG	1650

FIG.4B

AAGGCAGGGGACCCATGGCGAGGAGTGGCCAGCACCCCAGGCAGTCTGTGTGAGGCATAGCCCCTGGACACACA	1729
CACACAGACACACACACTGCCTGGATGCATGTATGCACACACA	1808
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CCCCCTGACACAGAGAAGGGGCCTTGGTATTTATATTTAAGAAATGAAGATAATATTAATAAT	2914
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              44
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                 v++eD+ G+Y C +
              89 VEREDA-GVYVCKA
       M003
                                 101
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                    M003
             165
                   GSSVRLKCVAS-GHPrPdITWMKDDQaltrpeaaeprkkkWTLSLk 209
                 svtpeDsgGtYtCvv<-*
                 +++peDs G YtC+v
       M003
             210 NLRPEDS-GKYTCRV
                                  223
ig: domain 3 of 3, from 261 to 340: score 26.9, E = 8.8e-07
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       M003
             261
                   GGTTSFQCKVR—SDVkPvIQWLKRVEygaegrhnstidvqqqkfvv 305
                 ......Islti.svtpeDsgGtYtCvv<-*
                 ++++ +++++
                                1+i+++++D+ G Y C
       M003
             306 lptgdvwsrpdgsylNKLLltRARQDDA-GMYICLG 340
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neur\_chan: domain 1 of 1, from 388 to 397: score 1.4, E = 9.7

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FIG.7

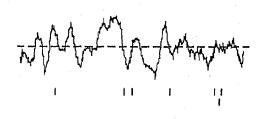
Input file M003jfmjf004c11; Output File M003jfmjf004c11.pat Sequence length 1074

										N AAC	K AAG	19 59
											N AAT	39 119
											P CCA	
										I ATC	G GGC	79 239
											K AAG	99 299
										G GGG	T ACA	119 359
										E GAG	E GAG	139 419
										P	K AAG	159 479
											H CAC	179 539
									_	A GCT	K Aaa	199 599
-		P		•	-							209

# FIG.8A

FIG.8B

PFAM



Cys Ngly

1 41 81 121 161 201

FIG.9

Input file M347Alhbad295g12; Output File M347Alhbad295g12.pat Sequence length 1423

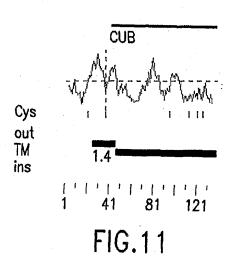
GTC	GACC	CACG	CGTC	CGCC	CACG	CGTC	CGG .		P CCT											12 66
									G GGC									_	V GTC	32 126
									V GTC										L CTG	52 186
									G GGC										K AAG	72 246
									V GTC		-								Q CAG	92 306
																			C TGT	112 366
									K AAG			_			-		-		R AGG	132 426
			F TTT																	139 447
GGG	CAGTO	CGGG(	CTTG	GCTT/	ACCG(	GGGAC	CAG	rgg t(	GGAC	CCCA	GGAC	ACAG	CCTC	CCAC	CAGC	GCCT	CCGG	GGCT	GCCA	526
TCTO	GGCC	CCAC	CAGAC	CAAA	\GAG(	GCAG	CAAC	CAG(	eccc.	rgcg <sup>.</sup>	TTTG(	GAAG	GCTT	ATGA/	ATGG	ACAC	ACAA	ATCT	TGCA	605
AAT(	TATO	GAG	CCAGO	GGCA	AGGG/	\CGC#	CATA	ATTG(	GTTG.	ΓΤΑΑ	AAAT	ATGT	CATC	ATGT	ATTT	GTTG	AGTG	CCTG	стст	684
ATC/	GGTC	SAGG/	AGC1	rgga(	CACA	<b>AATAA</b>	TAAC	CAAA	AGAT.	TAAG'	TCAC	CGTT	CACA	CTTA	CCTT	GGAA	GAGC	TATT	ACAA	763
AAC:	TCTA	AACG(	CAAA	AGCC1	TAT	CAGA	ATA	AGGA(	CATT	TAA	AAAC	AGTA	CTTG	ATGG	AGTG.	ATGC	AAGC	TTGC	AGTC	842
CCA(	CAG1	TATAC	TCAG	GAGA	CTG/	AGGCT	GGAG	GAT	CAGAC	GGC	TGGA	GCCC	AGGG	TTCA	AĞĞC	CAGC	CTAA	GCAA	CATA	921

# FIG.10A

GCAAGACCCCATCTCAAAAATAAGTAAATAAATAAAAATAAAAAGAGCACATTATCTTTTGATTTAAATTTTATTT	1000
NTATCAAAATGACATAAATTTTTGAACTTTATTTTTTAATTTTTAAAATTTTTAATTATTATGGATACATAATAGTTGTA	1079
AGACTTTTTGTTTTTTAATTAAAGTTTTCTAAGGCTGGGCGCAGTAGCTCATGTCTGTAGTCCCAGCACTTTGGGAGGC	1158
GAGGCGAAAGAAGCACTTGAGCCCAGGAATTTGAGACCAGCCTGGGCAACATAGCAAGACCCCATCTCTACAAAAAAA	1237
TTAAAAATTAGCCAAGTGTGGTGGCACGCACCTGTGGTCCCAGCTACAAGGGACGCTGAAGTGAGAGGATCACTTGAG	1316
CCTGGAAGGTAGAGGCTGCAGTGAGCTCTGATCATGACACCGTACTCCAGCCTGGGTGACAGAGTGAGACCCTGTCTCC	1395
NAAAAAAAAAAAAAAAAGGGCGCCCGC	1423

FIG.10B

M347



```
CUB: domain 1 of 1, from 40 to 136: score -17.7, E = 0.035
                 *->CGgtldltessGsisSPnYPnrsdYppnkeCvWrlrappgyrvVeLt
                                                    I ap+g+ V L
                     G +I+ +e + ++SP+YP+ +Y +e
      hM347
               40
                    -GSVLLAQELPQQLTSPGYPE--PYGKGQESSTD1KAPEGFA-VRLV 82
                 FqdFd1EdhdgapCryDyvEirDGdpss.p11G....rfCG....sgkPe
                 FqdFdIE +++ C+ D+v + G ++s++ G++++ CG+ + ++P
      hM347
              83 FQDFDLEPSQD—CAGDSVTVSWGWGGSrQDCGqgdsRGCGkwrcPESP- 129
                 dirStsnrmlikFvsDasvskrGFkAty<-+
                            + +D+
              130 -----F
      hM347
                                               136
```

FIG. 12

Input file T272Athda89h3; Output File T272Athda89h3.pat Sequence length 5036

GTC	GACC	CACG	CGTC	CGCT	CGAA	GCGG	GGAC	CCTC	GCCC	CGTC	CTCG	CCTC	TCCA	GTCC	TCCT	ссто	GCAG	ACCC	CGGC	79
GGT	TCCT	ACCC	CAGG	CCGC	AGGG	GAGA	CGGT	CCC	CAAG	GCAG	GCTT	CATA	TCCT	GAAC	GCTG	GGAT	CCCC	CAGG	ACAT	158
TCC	CTGG	CCCC	CAGG	CCCC	AGGT	CCCA	GCC	CCAG	GCTO	GAGC'	TGTG(	GGCA	GCC	CCAC	CTGG	CCTC	TGCA	M ATG	S TCA	2 235
																	T ACT			22 295
																	K AAG			42 355
																	E GAG			62 415
																	S TCA			82 475
																	P CCT			102 535
			L					-								P CCT	S TCC	L CTG	A GCC	122 595
			H CAC												L CTG		C TGC		H CAT	142 655
																	V GTC		G GGC	162 715
																	D GAC			182 775
																	C TGC			202 835

# FIG.13A

Q C H G A P C D P Q TG 222 A C CGC TGC CAG TGC CAT GGG GCA CCC TGC GAT CCC CAG ACT GGA GCC TGC TTC TGC CCC GCA 895 S C Р D V S C S Q G T 242 GAG AGA ACT GGG CCC AGC TGT GAC GTG TCC TGT TCC CAG GGC ACT TCT GGC TTC TTC TGC 955 THPCQNGG V F Q T P Q G 262 CCC AGC ACC CAT CCT TGC CAA AAT GGA GGT GTC TTC CAA ACC CCA CAG GGC TCC TGC AGC 1015 G T I C S L Ρ C Ε 282 TGC CCC CCT GGC TGG ATG GGC ACC ATC TGC TCC CTG CCC TGC CCA GAG GGC TTT CAC GGA 1075 S QE C C G 302 R Н N G L C D R F CCC AAC TGC TCC CAG GAA TGT CGC TGC CAC AAC GGC GGC CTC TGT GAC CGA TTC ACT GGG 1135 R C P G Υ Ţ G D R 322 С CAG TGC CGC TGC GCT CCG GGT TAC ACT GGG GAT CGG TGC CGG GAG GAG TGC CCG GTG GGC 1195 Ε T C 342 D C A D C A P D A R C CGC TTT GGG CAG GAC TGT GCT GAG ACG TGC GAC TGC GCC CCG GAC GCC CGT TGC TTC CCG 1255 C E Н G F T D R C 362 G Τ GCC AAC GGC GCA TGT CTG TGC GAA CAC GGC TTC ACT GGG GAC CGC TGC ACG GAT CGC CTC 1315 S С G L Q Α Р C 382 TGC CCC GAC GGC TTC TAC GGT CTC AGC TGC CAG GCC CCC TGC ACC TGC GAC CGG GAG CAC 1375 H P M N G E C S C L 402 AGC CTC AGC TGC CAC CCG ATG AAC GGG GAG TGC TCC TGC CTG CCG GGC TGG GCG GGC CTC C Ρ Q D T H G P G C 422 CAC TGC AAC GAG AGC TGC CCG CAG GAC ACG CAT GGG CCA GGG TGC CAG GAG CAC TGT CTC 1495 G V C Q Ţ S 442 Α G L C Q C TGC CTG CAC GGT GGC GTC TGC CAG GCT ACC AGC GGC CTC TGT CAG TGC GCG CCG GGT TAC 1555 СРР S 462 A S L D T. Y ACG GGC CCT CAC TGT GCT AGT CTT TGT CCT CCT GAC ACC TAC GGT GTC AAC TGT TCT GCA

## FIG.13B

GE 482 NAIACSP D CCC TGC TCA TGT GAA AAT GCC ATC GCC TGC TCA CCC ATC GAC GGC GAG TGC GTC TGC AAG 1675 502 R G N C S Ρ C GAA GGT TGG CAG CGT GGT AAC TGC TCT GTG CCC TGC CCA CCC GGA ACC TGG GGC TTC AGT 1735 S 522 С Н E A V C Α TGC AAT GCC AGC TGC CAG TGT GCC CAT GAG GCA GTC TGC AGC CCC CAA ACT GGA GCC TGT 1795 542 H G AHCQLP Ρ ACC TGC ACC CCT GGG TGG CAT GGG GCC CAC TGC CAG CTG CCC TGT CCG AAG GGG CAG TTT 1855 562 S R C D C D H S D GGA GAA GGT TGT GCC AGT CGC TGT GAC TGT GAC CAC TCT GAT GGC TGT GAC CCT GTT CAT 1915 Q A G W M G С H L S 582 A R GGA CGC TGT CAG TGC CAG GCT GGC TGG ATG GGT GCC CGC TGC CAC CTG TCC TGC CCT GAG 1975 602 N C S C С K G G GL N Ţ GGC TTA TGG GGA GTC AAC TGT AGC AAC ACC TGC ACC TGC AAG AAT GGG GGC ACC TGT CTC 2035 622 CVCAPGFRGPSC 2095 CCT GAG AAT GGC AAC TGC GTG TGT GCA CCC GGA TTC CGG GGC CCC TCC TGC CAG AGA TCC 642 R Y G K R C V P C K С Α N TGT CAG CCT GGC CGC TAT GGC AAA CGC TGT GTG CCC TGC AAG TGC GCT AAC CAC TCC TTC 2155 662 T C Υ C L A G W TGC CAC CCC TCG AAC GGG ACC TGC TAC TGC CTG GCT GGC TGG ACA GGC CCC GAC TGC TCC 2215 682 G H W G ENCAQ T C CAG CCA TGC CCT CCA GGA CAC TGG GGA GAA AAC TGT GCC CAG ACC TGC CAA TGT CAC CAT 2275 702 Н D G C Q S C 1 Ρ G GGT GGG ACC TGC CAT CCC CAG GAT GGG AGC TGT ATC TGC CCC CTA GGC TGG ACT GGA CAC 2335 LEGCPLGTFGANC S 722 CAC TGC TTA GAA GGC TGC CCT CTG GGG ACA TTT GGT GCT AAC TGC TCC CAG CCA TGC CAG 2395

FIG.13C

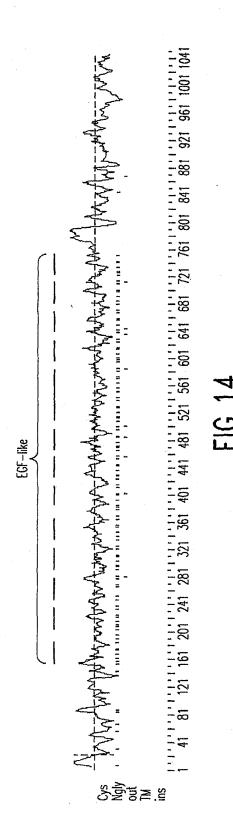
E K C H P E T G A C V C P P G H 742 TGT GGT CCT GGA GAA AAG TGC CAC CCA GAG ACT GGG GCC TGT GTA TGT CCC CCA GGG CAC 2455 1 G IQEPFTVM РТ 762 AGT GGT GCA CCT TGC AGG ATT GGA ATC CAG GAG CCC TTT ACT GTG ATG CCG ACC ACT CCA 2515 G Α ٧ I G 1 A V L G 782 GTA GCG TAT AAC TCG CTG GGT GCA GTG ATT GGC ATT GCA GTG CTG GGG TCC CTT GTG GTA 2575 ALFIG YRHWQKG K E 802 GCC CTG GTG GCA CTG TTC ATT GGC TAT CGG CAC TGG CAA AAA GGC AAG GAG CAC CAC 2635 V A Y S S G RLDGSE 822 Y V M CTG GCT GTG GCT TAC AGC AGC GGG CGC CTG GAC GGC TCC GAG TAT GTC ATG CCA GAT GTC 2695 YYSNPS S Н 842 Υ Н Т L S CCT CCG AGC TAC AGT CAC TAC TAC TCC AAC CCC AGC TAC CAC ACC CTG TCG CAG TGC TCC 2755 PNP N K ٧ PGP LFASL 862 CCA AAC CCC CCA CCC CCT AAC AAG GTT CCA GGC CCG CTC TTT GCC AGC CTG CAG AAC CCT. 2815 E R P G G A Q G H D N H T T L P A D W 882 GAG CGG CCA GGT GGG GCC CAA GGG CAT GAT AAC CAC ACC ACC CTG CCT GCT GAC TGG AAG 2875 P G ΡL DRGSSRL 902 CAC CGC CGG GAG CCC CCT CCA GGG CCT CTG GAC AGG GGG AGC AGC CGC CTG GAC CGA AGC 2935 YS N G PGPFYDKG 922 TAC AGC TAT AGC TAC AGC AAT GGC CCA GGC CCA TTC TAC GAT AAA GGG CTC ATC TCT GAA 2995 V A S L S S E N PY 942 GAG GAG CTC GGG GCC AGT GTG GCT TCC CTG AGC AGT GAG AAC CCA TAT GCC ACC ATC CGG 3055 DLPSLPGGPRESSYME 962 GAC CTG CCC AGC TTG CCA GGG GGC CCC CGG GAG AGC AGC TAC ATG GAG ATG AAA GGC CCT Р R 0 PPQFW 982 D S 0 CCC TCA GGA TCT GCC CCC AGG CAG CCT CCT CAG TTT TGG GAC AGC CAG AGG CGG CGG CAA 3175

FIG. 13D

P Q P Q R D S G T Y E Q P S P CCC CAG CCA CAG AGA GAC AGT GGC ACC TAC GAG CAG CCC AGC CCC	
D S V G S Q P P L P P G L P P GAC TCT GTG GGC TCC CAG CCC CCT CTG CCT CCG GGC CTA CCC CCC	G H Y D S 102 GGC CAC TAT GAC TCA 329
P K N S H I P G H Y D L P P V CCC AAG AAC AGC CAC ATC CCT GGA CAT TAT GAC TTG CCT CCA GTA	R H P P S 104 CGG CAT CCC CCA TCA 335
P P L R R Q D R * CCT CCA CTT CGA CGC CAG GAC CGT TGA	105 338
GGAGCCAGGATGGTATGGCAGAGGCCAGCACACCTGGCTGTTGCTGCTCAAGGCTGGGGA	CAGAGCCTAGTGTACCCCT 346
GCCAGGAGCAGGGAGTGGACCGGCAGGCTGTGAACATGAACAACGCTTAACAGAGCAAGT	GATGGGAGCCTTGTTCCTG 354
GGTTCTACCATGGGAGACGCTGATCAGCAGGATGCCTGGCTCCCTTTCCCAACCCACTGC	TCCCAAGGCCTCCAGGGCC 361
CTGTGTACATAAACTGGTGGGTTGGAAGTTGCTGGGTAACTCTGATTTCAGACATGCGTG	TGGGGTACCTTTTCTGTGC 369
ATGCTCAGCCTGGGCTCTGTGCGTGTGTGTTTCTGTGATTTTAGAAGGGTACCAGGCA	GGTTCTGTCCTAGGGCACT 377
TACCATTTAGTAGGGAGATGGAACCAACCCAATTAACTCTAGCAATAGCCTCCTAACTGG	CCTCCTCCATTGATTCAGT 385
GAACCTTCCAATGCATGGCTCATAATTTCAAAATACAGGCTGGTTAGTTA	GAAAGCCTTCATAGGTGCC 393
TCTTTGCTCTTCTGCCAGTATCAAAACTTTTGAAGGCCTTAAAGGCCCTGCTTTGCCTGG	CCCATCTGTCTCTCCAGCC 401
TCACCTTGAACTGTGTTCCTGTCACTGCACGCCAGTCACACCGGCCTCTAGGTCCTCCTG	TAGGCCACTCTTCTTTCTG 409
GCACAGGGACCTGCACACCTGGAGTGCCCTTCCTCCCCCACTCGCCTGTTCACCCCTGCT	TTTCCTTTACACCTCCTCC 417
TCAGGGAAGTGCCCACCCTCCGTACATCTTTCACAGCCCTGATTGCAGCTGTGTTCACTCA	ACCAGGTACCTGCAGAAGG 425
CCTACAGGGTGCCAGGCACTTCTTTAATGGGTTCTTTCTT	CTCTGCCTCCCCCACTAGA 433
CTGTAAGCTCCCTGAAGGCAAGAATCCTGTGCTTATGCTCAATATTAGCTCTCCCTTGGCA	ACAGAGTAGGCACTCAACA 440
AATGCTCCCCAAAAGGCTGAGTGGCTGACTGAATTAAGTACCAGTGACATGCAGTAACTGC	CTAAGATAGATGAGCCATC 448

FIG.13E

FIG.13F



EGF: domain 1 of 14, from 151 to 181: score 14.0, E = 1.2

\*->Capnn..pCsngGtCvntpggssdnfggytCeCppGdyyIsytGkrC C p++ + C + G+Cv +C+C pG + G++C hT272 151 CVPLCaqECVH-GRCVAPN------QCQCVPG-----WRGDDC 181

EGF: domain 2 of 14, from 200 to 229: score -2.2, E = 36

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyylsytGkrC<-C+ + C++ + C + g C+Cp tG+ C hT272 200 CQFRCQCHG-APCDPQTG------ACFCPAE-----RTGPSC 229

EGF: domain 3 of 14, from 242 to 272: score 16.0, E = 0.81

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyyIsytGkrC<-C+++ pC+ngG+ + g +C CppG + G C hT272 242 CPSTHPCQNGGVFQTPQG-----SCSCPPG----WMGTIC 272

EGF: domain 4 of 14, from 285 to 315: score 27.0, E = 0.00045

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyyIsytGkrC<-C++++ C+ngG C g +C+C+pG ytG+rC hT272 285 CSQECRCHNGGLCDRFTG-------QCRCAPG-----YTGDRC 315

FIG. 15A

EGF: domain 5 of 14, from 328 to 358: score 18.0, E = 0.22

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyylsytGkrC<-Ca+++ C +++C + g C C +G +tG+rC hT272 328 CAETCDCAPDARCFPANG-------ACLCEHG-----FTGDRC 358

EGF: domain 6 of 14, from 378 to 404: score 7.4, E = 4.9

\*->CopnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<-C+ + C++ g +C C pG ++G +C hT272 378 CDRE----HSLSCHPMNG-------ECSCLPG-----WAGLHC 404

EGF: domain 7 of 14, from 417 to 447: score 29.2, E = 9.3e-05

\*->CopnnpCsngGtCvntpggssdnfggytCeCppGdyyIsytGkrC<-C++++ C++gG+C+ t g C+C+pG ytG++C hT272 417 CQEHCLCLHGGVCQATSG------LCQCAPG-----YTGPHC 447

EGF: domain 8 of 14, from 460 to 490: score 6.0, E = 6.5

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyyIsytGkrC<-C+ + C n C + g +C+C++G ++ +C hT272 460 CSARCSCENAIACSPIDG------ECVCKEG-----WQRGNC 490

FIG.15B

EGF: domain 9 of 14, from 503 to 533: score 15.9, E = 0.82

\*->CopnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<-C+ + C + ++C + g C+C+pG ++G +C hT272 503 CNASCQCAHEAVCSPQTG------ACTCTPG-----WHGAHC 533

DSL: domain 1 of 1, from 518 to 576: score -20.5, E = 6.8

yt.Cd.enGnklCleGWkGeyC<-\*
+ +Cd+ +G+ +C +GW+G C
hT272 555 SDgCDpVHGRCQCQAGWMGARC 576

EGF: domain 10 of 14, from 546 to 576: score 11.7, E = 2

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<-Ca+ + C++ C +++g +C+C+ G + G rC hT272 546 CASRCDCDHSDGCDPVHG------RCQCQAG----WMGARC 576

EGF: domain 11 of 14, from 589 to 619: score 17.9, E = 0.24

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<-C+ ++ C+ngGtC++ g C+C+pG + G+ C hT272 589 CSNTCTCKNGGTCLPENG------NCVCAPG-----FRGPSC 619

FIG.15C

EGF: domain 12 of 14, from 632 to 661: score 18.0, E = 0.23

\*->CopnnpCsngGtCvntpggssdnfggytCeCppGdyyIsytGkrC<-C p C n+ +C+++ g tC C G +tG++C hT272 632 CVPC-KCANHSFCHPSNG-----TCYCLAG-----WTGPDC 661

EGF: domain 13 of 14, from 674 to 704: score 27.1, E = 0.00042

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<-Ca+++ C++gGtC++ g +C+Cp G +tG++C hT272 674 CAQTCQCHHGGTCHPQDG------SC1CPLG----WTGHHC 704

EGF: domain 14 of 14, from 717 to 747: score 1.7, E = 16

\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyylsytGkrC<-C++++ C g +C++ g C+CppG +G C hT272 717 CSQPCQCGPGEKCHPETG------ACVCPPG-----HSGAPC 747

FIG.15D

Input file t272Atmzb62c4; Output File t272Atmzb62c4.pat Sequence length 2569

S CG A										19 58
									N AAC	39 118
C TGT									A. GCA	59 178
G GGG										79 238
V GTG										99 298
C TGC										119 358
L CTC										139 418
S AGC										159 478
M ATG										179 538
E GAG										199 598
Q CAG										219 658
I TTA										239 718

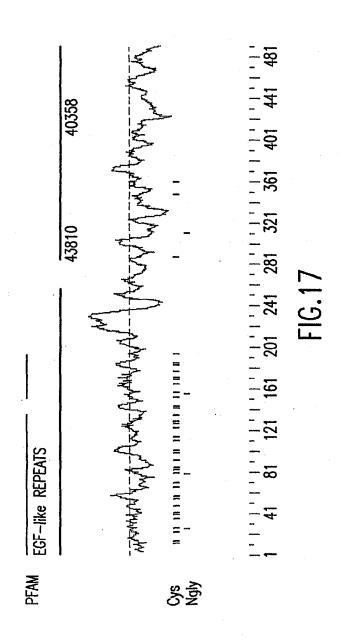
# FIG. 16A

WQKGKEHEHLAVAYST 259 TAC CGC CAG TGG CAA AAG GGC AAG GAA CAT GAG CAC TTG GCA GTG GCT TAC AGC ACT GGG. 778 S D Y V M PD V S Р S 279 Υ CGG CTG GAT GGC TCT GAT TAC GTC ATG CCA GAT GTC TCT CCG AGC TAT AGT CAC TAC 838 PSY Н TLS Q C S P N 299 TCC AAC CCC AGC TAC CAC ACA CTG TCT CAG TGT TCT CCT AAC CCC CCG CCC CCT AAC AAG 898 GSQLFVSSQAP Ε R 319 GTC CCA GGC AGT CAG CTC TTT GTC AGC TCT CAG GCC CCT GAG CGG CCA AGC AGA GCC CAC 958 £ T L P A N T - D K Н 339 R GGG CGT GAG AAC CAT ACC ACA CTG CCC GCT GAC TGG AAG CAC CGC CGG GAG CCC CAT GAC 1018 S HLD R S Y S C S Y S Н R N G 359 AGA GGC GCC AGC CAC CTG GAC CGA AGC TAT AGC TGT AGC TAT AGC CAC AGG AAT GGC CCA 1078 GPFC E н к G PIS E G L G 379 GGA CCA TTC TGT CAT AAA GGT CCC ATC TCT GAA GAG GGA CTA GGG GCA AGC GTT ATG TCC 1138 N P Y A T I R D L P S L PGE 399 CTG AGC AGT GAG AAC CCC TAT GCT ACC ATC CGA GAC CTG CCC AGC CTG CCT GGG GAA CCC 1198 Ε S S M K G Р Р Р 419 CGA GAA AGT GGC TAT GTG GAG ATG AAA GGA CCT CCA TCA GTG TCC CCT CCC AGG CAG TCT 1258 0 R 0 0 Р Q-R 439 CTT CAT CTC CGG GAC AGG CAG CAG CGG CAA CTG CAG CCA CAG AGG GAC AGC GGC ACC TAT 1318 SHNEE SLG S 459 GAG CAG CCC AGC CCC TTG AGC CAT AAT GAA GAG TCT TTG GGC TCC ACG CCC CCG CTT CCT 1378 PPG S P K Н 479 Y D N S CCA GGC CTG CCT CCT GGT CAC TAC GAC TCC CCC AAG AAC AGC CAT ATC CCT GGA CAC TAT 1438 RHPPSPPS 498 R R Q GAC TTG CCT CCA GTA CGG CAT CCT CCA TCC CCT CCA TCC CGG CGC CAG GAC CGC TGA 1495

## FIG.16B

AGAGCCGCCATGGTATGGGAGCGTGCCTATGTACCTTGCCAGGAGCAGCGACTGGACCAGCAGGCCACGAACAGAAACA CTTGGTGAAGTGAACAGAGACAGACTGTGGCCCTGTGCTTCCACCGAGGGAGACACTAGTTGACAAAGTGTCTAACCCT 1653 CTTTTCCAACCCACTGCTCAAGTCCCTGTGGACATAAGCTGGTGGCCAGAATGTTGTTGTACAAGTGTGATTTTAGATC 1732 1811 AGAGGGAGTCAGGTATAGGTTCTGCCTTCTGCACTTTCCATCTTATCTAGTAGTCAGCTTCCAAGCTTAACTAGTTAGA 1890 GCTCCACCAGCAGCAGCCCTAACTACCTGCCTGCCCTTCACCCAGTAATCCTCCATGTCTTTGCTCAGAGGATTGCTC 1969 CCCGACTCTGGTGTTGTCCTCCTGGTACGCCTTGACGGTCCTGCAGTCTCCCTTTCCCGTCTTGCTTCATTCTTTCCCA 2048 GAATGAAGGCTGTCTGCCACCCTACTTCCCAGCCCAGGAATTGGCACATCTAAGTTCAGCCTTACTAAGTTACCCGTTG 2127 2206 ACAGAAGGCAGAAGTGGTACCAGGCAAGAAGATGGGATTGTTGCATTTTGTTTTTTGAGACTCTGTCTCACTATG 2285 TGCACAGCTCAAGCTGCACTCCGATGTGCTTTCCCCTGTTGCTAGATTAGCGTCTGCCTCCCCCTAGTGGAGAGGCTGA 2522 2569

FIG.16C



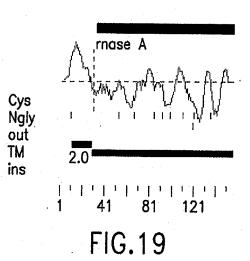
•			295F ngth	•		); UL	ıtput		e 12	(9DAT	.nyoz	(309.	pat							
STC	GACC	CACG	CGTC	CGGC	TCCC	AGCCI	CACC	CCCA	AACA(	GACA	CAGC	GTAG	CCCG	GGCC	AGCT	CTTA	AGGA	GTTC	AGGA	79
GTG/	AGAA	GAGG	CCCT	CAGA	GATC	TGAC	AGCC	TAGG	AGTG(	CGTG(	GACA	CCAC	CTCA	GCCC	ACTG	AGCA	GGAG	TCAC	AGCA	158
CGA	AGAC(	CAAG	CGCA	AAGC	GACC	CCTG	CCCT	CCAT	CCTG	ACTG(	CTCC	TCCT	AAGA	GAG /					R AGA	
																	E GAG		P CCA	25 291
																			Q CAG	45 351
																			C TGC	65 411
																			T ACC	
																	P		S TCC	105 531
																	E GAG		R CGA	125 591
																	Q CAG		F TTC	145 651
			P CCT						V GTC											157 687

# FIG.18A

GTTTCCAGACTGGCTTGCTCTTTGGCTGACCTTCAATTCCCTCTCCAGGACTCCGCACCACTCCCCTACACCCAGAGCA	766
TCTCTTCCCCTCATCTCTTGGGGCTGTTCCTGGTTCAGCCTCTGCTGGGAGGCTGAAGCTGACACTCTGGTGAGCTGA	845
GCTCTAGAGGGATGGCTTTTCATCTTTTTGTTGCTGTTTTCCCAGATGCTTATCCCCAAGAAACAGCAAGCTCAGGTCT	924
STGGGTTCCCTGGTCTATGCCATTGCACATGTCTCCCCTGCCCCTGGCATTAGGGCAGCATGACAAGGAGAGAAATA	1003
NATGGAAAGGGGGCATATGGGATTTGTGGACACAGCTGTTTCTGTTCCTGAACTAGAAGTCTTCCCCAGCTCTGACGTG	1082
CAGTGAGGTGACCTGAAGGAAAGAAAAATATAAATAAATA	1161
ACATAGACTTGACAGGGATTGTATGCCTTCTTTATGGATGAGGAAATTAAGGTTTTAGAAAGCTTAATGAATTAAAGAG	1240
CTTGTCTAATTAGTTAGTAGCAGAACCTGGACTTGAACCTAGGTCTCCTTGCTCTAAATACAGTGTACCTTCTACTCTA	1319
CCAGTTGCGCAAGAAAGAAGTCACTGTTACAGAGGCAAGCGGTGAACTAGGTAAGAGTTCACTCATGAAGAAACGAGTG	1398
CTCTGAAGAGCCAGTTACCCTGTGTTGGCTGCAATAAAGGTCATTACCTCTCTAGCCAAAAAAAA	1477
AAAAAAAAAAAAAAAA	1497

FIG.18B

T295



32	*->qesrAqkFIrQHiDspktsssnpnYCNqMMdkrRnmtqgrCKpvNTF + ++ q+F++QH+ ++s + CN +M k++n rCK+ NTF GMTSSQWFKIQHMQPSPQACNSAM-KNINKHTKRCKDLNTF	71
72	vHesladVkaVCsqkNvtCkNGqkNCyqSkssfqiTdCrltggsqkyPnC +He++++V a C ++ + CkNG kNC+qS+ +++++T C+lt+g yPnC LHEPFSSVAATCQTPKIACKNGDKNCHQSHGPVSLTMCKLTSGKYPNC	119
120	rYrtsastkhIiVACEgrd.rddPyynPyvPVHFDasv<-* rY+ + ++k ++VAC +++++d+ ++ vPVH+D++ RYKEKRQNKSYVVACKPPQkKDSQQFH-LVPVHLDRVL 156	

FIG.20

Input file T354Athla42a4; Output File T354Athla42a4.pat Sequence length 1788

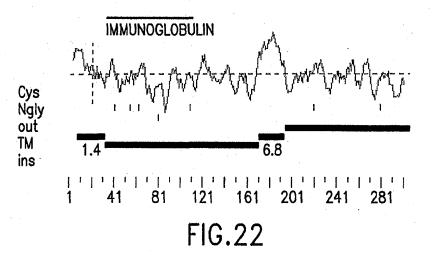
GTO	ርልሮር	ር ልርር፣	GCGT	orac.	ቦሮ ለር፤	ድድፕሮ	ጉል ጉፕ	C ACC	COAA	rccc	ርልሮሮ	TOTO	TC A A	CACA		M i		_	_	4 73
GIO	UNICO	OACO.	0001		CCAG	0010	UNO I	JAGG	JUNN	COGO	JACC	1010	IUAA	ONON	א טא	10 0		10 0	10	/3
			L																	24
ACA	CTC	TAC	CTG	CTC	CTC	TTC	TGG	CTC	TCA	GGC	TAC	TCC	ATT	GCC	ACT	CAA	ATC	ACC	GGT	133
Р	Ţ	. Т	٧	N	G	ı. E	F	R	G	S	ı	Т	v	O	С	V	Υ	R	S	44
			GTG																	193
. ^	147	۲.	T	v		1/	ш	100	^	ο.	^		,	141					•	64
			ACC															K		253
			T			,														84
CII	GII	AAA	ACC	AG I	GGG	ICA	GAG	CAG	GAG	GIG	AAG	AGG	GAC	CGG	GIG	TCC	AIC	AAG	GAC	313
N	Q	K	N	R	T	F	T	٧	T	М	E	D	L	М	K	T	D	A	D	104
AAT	CAG	AAA	AAC	CGC	ACG	TTC	ACT	GTG	ACC	ATG	GAG	GAT	CTC	ATG	AAA	ACT	GAT	GCT	GAC	373
T	Y	w	С	G	1	F	K	T .	G	N.	D		G	V	т.	٧	0	v	T	124
			TGT																	433
				•				_						-	_	-			•	
			A GCG																	144 493
Α11	UNU	CUA	000	100	AÇ I	001	000	000	ACC	AUU	001	AUI	100	AC:	ACO	111	nun	OUN	COA	730
			Ε																	164
GTC	ACC	CAA	GAA	GAA	ACT	AGC	AGC	TCC	CCA	ACT	CTG	ACC	GGC	CAC	CAC	TTG	GAC	AAC	AGG	553
Ή	K	L	L	K	L	S	٧	L	L	Р	L	ī	F	Т	I	L	L	L	L	184
CAC	AAG	CTC	CTG	AAG	CTC	AGT	GTC	CTC	CTG	CCC	CTC	ATC	TTC	ACC	ATA	TTG	CTG	CTG	CTT	613
,	W	٨	A	c			A			1.4	L f	1/	v	^	^	1/		٨	^	204
			GCC																	673
			Ε															L		224
AIG	ICC	CCA	GAG	CAG	GIA	CIG	CAG	CCC	CTG	GAG	GGC	GAC	CTC	TGC	TAT	GCA	GAC	CIG	ACC	733

# FIG.21A

L CTG C														-		A GCC	-	-	244 793
D GAC C	Q V AG GT			_						S TCC	_			E GAG	D GAC	I ATT	_	Y TAT	264 853
A :		T G ACC	L TTG	-		E GAG	D GAT		E Gaa	P CCG		Y TAC	•	N AAC	M ATG	G GGC	H CAC	L	284 913
S :	S H GC CA	_	P CCC	G GGC	R AGG		P CCT		E GAG	P		E Gaa	Y TAC	S AGC	T ACC	I ATC	S	R AGG	304 973
P CCT T	* AG																		306 979
CCTGC	ACTCC.	AGGCT	CCTT	CTTGC	SACCO	CCAGC	CTG	rgag(	CACAC	CTCC1	rgcci	CATO	CGACC	CCTC	rgcco	CCTC	CTC	CCCT	1058
CATCA	GGACC	AACCC	GGGG/	ACTGC	STGC	стстс	CCTC	SATCA	AGCCA	\GCA1	TGCC	CCTA	AGCT(	CTGGC	GTTG(	GCT	rggg(	GCCA	1137
AGTCT	CAGGG	GCTT	CTAGO	GAGTT	rggg(	GTTT	CTA	NACG1	CCCC	CTCCI	CTC	CTACA	ATAG1	TTGAG	GAG(	GGGG	CTAG(	GAT	1216
ATGCT	CTGGG	CTTT	CATGO	GAA1	rgat(	SAAGA	TGAT	TAAT(	SAGAA	TAAA	IGTT/	ATCAT	ΓΤΑΤΊ	TATC/	\TGA/	GTA(	CAT	TATC	1295
ATAAT	ACAAT(	GAACC	TTTA	ΓΤΤΑΊ	rtgc(	CTACC	CACA1	GTTA	ATGGG	CTG/	\ATA/	ATGGC	cccc	CAAAC	ATA	CTG	GTC	CTAA	1374
TCCTC/	AGAAC	TTGTG	ACTG1	TACC	CTTCT	GTGG	CAGA	AAGG	GACA	GTGC	AGAT	GTAT	GTAA	GTTA	AGG/	CTTI	· ·GAG/	ATAG	1453
AGAGG'	TTATT	CTTGC	TGATI	r <b>C</b> AGG	TGGC	CCC/	LAAA1	ATCA	CCAC	AAGO	GTCC	CTCAT	AAGA	AAG/	GGCC	CAGA/	AGG TO	CAAA	1532
GAGGT	AGAGA	CAAAG	TGATO	SATGO	SAAG	rggac	GTGC	GTGT	GACG	TGAG	CAGG	GGCC	CATGA	\ATG(	CGCA	AGCC1	TCA(	SATG	1611
CCAGA	AAGGG/	AAAGG.	AATGG	SATTO	CCCC1	GCCT	GGAG	CCTC	CAAA	AGAA	VACC#	GCCC	CTGCC	CACG	CCTI	GACT	TGAG	CCC	1690
ATTGA/	AACTG/	ATCTTO	GAGCT	ССТО	GCC1	CCAG	TAAT	GCAG	GAGA	ATAA	ATTI	GTGT	TGTT	TTTA	AAA/	\AAA!	\AAA	<b>NAAA</b>	1769
<b>4</b> AAA(	GGGCG(	CCGC	TAGA																1788

# FIG.21B

T354



```
*->GesvtLtCsvsgfgppgvsvtWyf....kngk.lgpsllgysysrl
++s+t +C ++ + + +++ W+ ++ ++ k l ++ s +

RGSLTVQCVYR--SGWETYLKWWCrgaiwRDCKiLVK--TSGSEQEV 75

esgekanlsegrfsis.....sltLtissvekeDsGtYtCvv<-*
++ r+si ++++++++++++++ k D+ tY+C

76 KRD-------RVSIKdnqknrTFTVTMEDLMKTDADTYWCGI 110
```

FIG.23

Input file T378Athta28f4; Output File T378Athta28f4.pat Sequence length 3258

															9 68				
															E Gaa				29 128
															S TCC				49 188
															N AAC				69 248
															S TCT			L CTG	89 308
T ACC			T ACT			R CGG									A GCC	R CGG	Q CAG	H CAC	109 368
A GCC															R CGC		_	L CTG	129 428
															E Gaa				149 488
															V GTG		_	R AGG	169 548
															Y TAC				189 608
															S AGC				209 668
															H CAC				229 728

# FIG.24A

MQLSPAL V P A E LL APL 249 GCT GTT CTC ATG CAA CTC TCC CCA GCC CTG GTC CCT GCA GAG TTG CTG GCA CCT CTT ACG 788 C S I S 1 V A S 269 L I TAC ATC TCC CTC GTG GGC TGC AGC ATC TCC ATC GTG GCC TCG CTG ATC ACA GTC CTG CTG 848 K 0 S D S LTRI Н 289 CAC TTC CAT TTC AGG AAG CAG AGT GAC TCC TTA ACA CGC ATC CAC ATG AAC CTG CAT GCC 908 IAFL LSPA 309 N TCC GTG CTG CTC CTG AAC ATC GCC TTC CTG CTG AGC CCC GCA TTC GCA ATG TCT CCT GTG 968 A L A A ALHYAL 329 CCC GGG TCA GCA TGC ACG GCT CTG GCC GCT GCC CTG CAC TAC GCG CTG CTC AGC TGC CTC 1028 Ε G F N L Υ LL L G Υ 349 ACC TGG ATG GCC ATC GAG GGC TTC AAC CTC TAC CTC CTC GGG CGT GTC TAC AAC ATC 1088 YIRRYVFKLG V L G WGAPALL 369 TAC ATC CGC AGA TAT GTG TTC AAG CTT GGT GTG CTA GGC TGG GGC GCC CCA GCC CTC CTG 1148 L S ٧ K S S Y G P C 389 ٧ GTG CTG CTT TCC CTC TCT GTC AAG AGC TCG GTA TAC GGA CCC TGC ACA ATC CCC GTC TTC 1208 G T G F S C 409 GAC AGC TGG GAG AAT GGC ACA GGC TTC CAG AAC ATG TCC ATA TGC TGG GTG CGG AGC CCC 1268 Υ 429 М G G G S GTG GTG CAC AGT GTC CTG GTC ATG GGC TAC GGC GGC CTC ACG TCC CTC TTC AAC CTG GTG 1328 Ε 449 A L W ĪL R R L R R GTG CTG GCC TGG GCG CTG TGG ACC CTG CGC AGG CTG CGG GAG CGG GCG GAT GCA CCA AGT 1388 H D T ٧ T ٧ L 469 G T GTC AGG GCC TGC CAT GAC ACT GTC ACT GTG CTG GGC CTC ACC GTG CTG GGA ACC ACC 1448 F S F G V F 489 F L Р F 1508

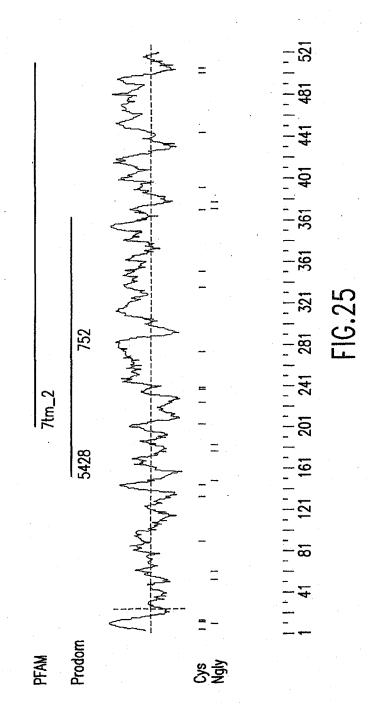
FIG.24B

509 ATC TTA AAC TCG CTC TAC GGT TTC TTC CTT TTC CTG TGG TTC TGC TCC CAG CGG TGC CGC 1568 S 529 F Ε Α. TCA GAA GCA GAG GCC AAG GCA CAG ATA GAG GCC TTC AGC TCC TCC CAA ACA ACA CAG TAG 1628 1707 TCCGGGCCTCCTGGCCTGGAATCCTCAGCCTCTCTGGCCGCCAGTAGCCTGAGGCTACGGCTCCTGCTAGAGAGGGTGG CAGGCCTGCTGCTGGACCCCAGAGGCCACTGTGACCGCCAAGGGGCCTTTTCCACTTCCACGCCTCTCCAGGCACTGA 1786 GGGGAAGGCATTGCTCTACCTCTCCCTGACATTTTGCTCCGGGCCAGATCCAACCTTACCTGGGCCAGCAAACTTTGTC 1865 CTGGTACCTGGGCCCAGCTCGCCAGGGATGTGGGCAGAGCACCAGCCTGGGCATCAGGAAGCCAAGTTTCAAGGACTGT 1944 CTTTGAGTCTGTCTGTATGACCTTGGGCCTGCCACTTCTCACAGACCCTAGGTATCCACAGCTGTGACATGGGGGCAAG 2023 CGGCTTTGTTTCAGCCTAACCCAGGAGCTTAGTAAAAATTGCATAAGACCAGGGGGAAGAGTGTCAGCGTGGGGTGGGA 2102 2181 ATTCCCGCGGCCTCCACCTGCTTGCTAGGGGCAGGATCTCATTCAGGCTGCCCTGGAAGCACCTGCTTGGCCCTGCACAC 2260 2339 ATGCCTGAGGCCTCTTTTCCTTTAACTCCCTAAATTATGATGACTCCAAGTCCAAGCCCACCCTTCCCAAAGATTGGGA GGTTCCGCCGTTCCCAGAGGCTCCTCCTGCGGTGCTCCCAAGACTTCCATAGACCATCTGGACCAGTAGCCCATCCCGC AGTTTTCTTGGGGGCAGAGCAAAACGCTTCTTTCTCCTCCAGCTGAATCAGCTGGATCCCAGTGTCCTGGCTGTTTGGT 2497 GATTGGGCAAGATTGAATTTGCCCAGGTAGCCGTGAGAGTGTGGGTTTTAAATTCGAAGCTCAGGCCATAGTTTCAGAG 2576 2655 GTTGGTCCACACTCAGAGGCCCTTGGCGCCAAGACTGCATCTAGAATCGCTCAAACACCTGTTTGCAGACCCCATGCAC 2734 CAGCTGGAGGGGCCGTAACTGCAGGACTGCGCCTACTGAGTGACCCATTTCCTCCAGGAGGAAAGGCAAGACACGCTTA CACGGCCATTTGTCTCTTTTCCCAATGCGGCGGTGCACTTTCGCTCTTGGGGGCTGCACCCCAGACATAGCTGGCACCA

FIG.24C

GAGCAGGGTGCTCAGGTGGTGGTGCTCAGGGCCCTGCCCCAGGCCACTGGGCCGTTTTGATGACCTCGAAGGTCACAG 2971
GCAGAAAATAGGAGCAGGATTTCCCCTGGGGAAAAGTTCTCCTGGGACATCTTCTGCTCTTCTGTACATTTCTAGATGC 3050
AAATAACTCCTTCACCAGGCAGTGAGTGGCGTAGGCTCTGGAGCCAGGCTGCCTGGGCTCCAATGCCAGCTCTGCCACT 3129
TGCTAGCTGTGAGACTGTGGACAAACCACTCAGCCTCTGTGTGCCTCAGTTTTCCTATTTGTAAAATAGAGGCCATAGT 3208
GGTACCTATTTTGAAGACTAAGTAAAAGAATTCAAATAAAGAGACTTGGC 3258

FIG.24D



187	*->CnrtWDgitCWpdtppGelVvvpCPkyfygfssdqtdttgn +tC W+ + ++++p+G ++ C ++q ++ LTCvfWKEGarkqPWGGWSPEGCRTEQPSH	216
217	<pre>vsRnCtedGsWsepppsNrtWrnysaCgeddpeeesekkkkyylvlkiiY ++ C+ + +++ + ++ + 1 +i SQVLCRCNHLTYFAVLMQLSPALVPAELLAPLTYIS</pre>	252
	$tv {\tt GYS1SLaaL1} v {\tt AvvIL11FR} k Lht {\tt lwpdnadgalevgapWGAPfqvrr}$	
253	+vG S+S++a 1+ v++ FRk + + + LVGCSISIVASLITVLLHFHFRKQSDSL	280
281	SirCtRNyIHmNLF1SFILrAasvfikdavlksevssdeperLssrcsls tR IHmNL +S +L +++ ++ a s v+ ++TRIHMNLHASVLLLNIAFLLSPAFAMSPVPGSA	313
314	tgqvvvgCkllvvfQfqYcvmtNffWlLvEGlYLhtLLvvtffsErkylw C +l ++ ++Y++++ +W+ +EG L+ LL + ++y + CTALAAA-LHYALLSCLTWMAIEGFNLYLLLGRVYNIYIR	352
353	wYllIGWGvPlVfvtvWaivRllfedtgCWdsnGLAmFPEAKmCiW Y+ + +++GWG+P++ v v++ ++ +C++++ F RYVfklgVLGWGAPALLVLLSLSVKSSVY-GPCTIPVFDSWENGTG	397
398	msdnshlwWIIkgPiLlsilVNFflFinIirILvtKLRaa n+++ W+ + P++ s+lV + ++ ++ N++++ ++ L + LR+ F-QNMSICWV-RSPVVHSVLVmgyggltslfNLVVLAWALWTL-RRLRER	444
445	<pre>qtgetdqrqYsqYrkLaKSTL1LIPLfGIhyvvFafrPsndarGv1rkik + + + + L L L+G++ + +f+++ v+ + ADAPSVRACHDTVTVLGLTVLLGTTWALAFFSFGVFLLPQ</pre>	484
485	<pre>lyfelsLgSFQGFfVAvlYCFlNgEVQaEirrrW&lt;-* l++ L+S+ GFf ++ F+ + ++E + LFLFTILNSLYGFFLFLWFCSQRCRSEAEAKA 516</pre>	

FIG.26

inputs	ATGACGC	10 CGAGCCCC	20 CTGTTGCTGC	30 TCCTGCTGCC	40 GCCGCTGCTG	50 CTGGGGGCC	60 TTCCCGCCGG	70 GCCGCCG
inputs			90 CAAAGATGGO					
inputs	GCGGCTG		160 :AGTGGAGGG					
inputs	CACAGCG	220 GCTGGAGO	230 CGCTTCCGCG		250 GGGGCTGAAG			
inputs	CCGGCGT	290 GTACGTGT	300 GCAAGGCCAC	310 CAACGGCTTC	320 GGCAGCCTGA	330 GCGTCAACTA	340 ACACCCTCGT	350 CGTGCT
inputs	GGATGAC	360 ATTAGCCC	370 AGGGAAGGAC	380 AGCCTGGGG	390 CCGACAGCTC	400 CTCTGGGGG	410 TCAAGAGGAC	420 CCCGCC
inputs			440 CGACCGCGCT CGTCCG					
inputs	TGGGTAG	500 CTCCGTG(	10 510 GGCTCAAGTO	520 GCGTGGCCAGO	530 GGGCACCCTO	540 GGCCCGACA	550 TCACGTGGAT	560 GAAGGA
inputs	CGACCAG	570 GCCTTGAC	580 CGCGCCCAGAG	590 GCCGCTGAGO	600 CCAGGAAGAA	610 GAAGTGGAC	620 ACTGAGCCTG	630 AAGAAC
inputs	CTGCGGC	640 CGGAGGA(	650 Cagcgcaaat	ACACCTGCCG		680 CGCGCGGGC	690 GCCATCAACG	700 GCCACCT

inputs	ACAAGGTG	10 GATGTGAT	720 CCAGCGGACC	730 CGTTCCAA	740 AGCCCGTGCTC	750 CACAGGCACGO	760 CACCCCGTGA	770 ACACGAC
inputs	7 GGTGGACT	80 TCGGGGGG	790 ACCACGTCCT	800 TCCAGTGC	810 CAAGGTGCGCA	820 AGCGACGTGAA	830 AGCCGGTGAT	840 CCAGTGG
inputs	CTGAAGCG	50 CGTGGAGT/	860 ACGGCGCCGA	870 GGGCCGCC	880 CACAACTCCAC	890 CATCGATGTG	900 GGCGGCCAG	910 AAGTTTG
inputs	TGGTGCTG	20 CCCACGGG CCCACGGG 20	ŗĠĀŢĠŢĠŢĠĠ	ŤĊĂĊĠĠĊĊ	950 CGACGGCTCC TĠĀTĠĠĊŤĊĊ 40	TÁCCTCÁÁCÁ	970 AGCTGCTCA AGCTGCTCA 60	980 TCACCCG TĊTĊĠ 70
inputs	TGCCCGCC, GĠĊĊĊĠĊĊ, 80	90 AGGACGAT ÁĠĠĀTĠĀŤ( 90	ĠĊŢĠĠĊĂŢĠŢ	ÄĊÄŤĊŤĠĊ	1020 CTTGGCGCCA CTAGGTGCAA 110	ÁTÁCCÁTGG	1040 CTACAGCTT CTACAGTTT 130	1050 CCGCAGC CCGTAGC 140
inputs	GCCTTCCT GCCTTCCT GCCTTCCT 150	60 CACCGTGC CACTGTAT 160	TÁCCAGACCC	1080 AAAACCGC CÅÅÅĊĊTĊ O	1090 CAGGGCCACC CAGGGCCTCC 180	1100 TGTGGCCTCC TATGGCTTCT 190	1110 TCGTCCTCG TCATCGTCA 200	1120 GCCACTA TĊĊĀĊĀĀ 210
inputs	GCCTGCCG GCCTGCCA 220	30 TGGCCCGTC TGGCCTGTC 230	GTGÁT CGGC	1150 ATCCCAGC ĀTĊĊĊĀĠĊ 0	1160 CGGCGCTGTC TĠĠTĠĊŤĠŤĊ 250	TTCATCCTAG	1180 GCACCCTGC GCACTGTGC 270	1190 TCCTGTG TGCTCTG 280
inputs	GCTTTGCC, GCTTTGCC, 290	ĂĠÁĊĊAÁĠ/	AĞAĞÇÇAT	ĠŢĠĊĊĊĊ	1230 GCGCCTGCCC ĠĊATĊTAĊAĊ 320	TŤĊĊŦĠŤĠĊĊ	1250 TGGGCACCG TGGGCATCG 340	1260 CCCGCCG TĊĊCĊĊĀ 350
inputs	GGGACGCC ĠĠĠĀĊĀŢĊ 360	ĊĊĠĄĠĂĄĊĠ	CAGTGGTGA	ĊĀĀĠĠĀĊĊ	1300 TTCCCTCGTT TGCCCTCATT 390	1310 GGCCGCCCTC  GGC 400	1320 AGCGCTGGC	1330 ccтggтg †Ġ
inputs	TGGGGCATA TĠĠĠCATA 410	ŤĠŤĠÁĠĠĂ	CATGGATCC	GĊCĂTĠĠĊ	1370 CCCCCAGCAC CCCCCAGCAC 440	AŤCĊŤĠĠĊĊT	ĊŦĠĠĊŦĊŔŔ	cŤĠĊŤĠĠ

## FIG.27B

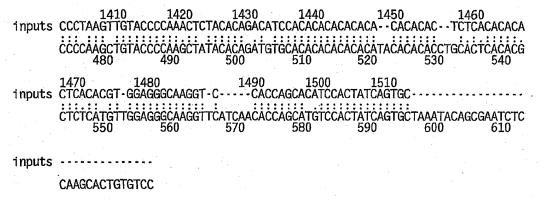


FIG.27C

970 GTGCTG ĠTCCGG	980 CCCACGGGTGA CCCACGGGTGA 20	990 CGTGTGGTCG TGTGTGTCA 30	1000 CGGCCGGAC CGGCCTGAT 40	1010 GGCTCCTACCT GGCTCCTACCT 50	1020 CAATAAGCTGG CAACAAGCTGG 60	1030 CTCATCACCCCTG CTCATCTCTCGGG 70
L040 CCCGCC	1050 AGGACGATGCG	1060 GGCATGTACA	1070 TCTGCCTTG	1080 GCGCCAACACC	1090 ATGGGCTACAG	1100 GCTTCCGCAGCGA GTTTCCGTAGCGC 140
1110 CTTCCT CTTCCT 150	1120 CACCGTGCTGC CACTGTATTAC 160	1130 CAGACCCAAA CAGACCCCAA 170	ÁCCTCCÁGG	1150 GCCACCTGTGG GCCTCCTATGG 190	1160 ccTccTcGTcc cTicTicAicc 200	1170 CTCGGCCACTAGC GTCATCCACAAGC 210
L180 CTGCCG CTGCCA 220	1190 TGGCCCGTGGT TĠĠĊĊTĠTĠĠ 230	1200 CATCGGCATC GATCGGCATC 240	1210 CCAGCCGGC CCAGCTGGT 250	1220 GCTGTCTTCAT GCTGTCTTCAT 260	1230 CCTGGGCACCC ĊĊŤÅĠĠĊĀĊTC 270	1240 CTGCTCCTGTGGC GTGCTGCTCTGGC 280
1250 TTTGCC, TTTGCC, 290	1260 AGGCCCAGAAG AGACCAAGAAG 300	1270 SAAGCCGTGCA SÁÁGCCÁTGTG 310	1280 CCCCCGCGC CCCCAGCATO 320	1290 CTGCCCCTCCC CTACACTTCCT 330	1300 CTGCCTGGGCA GTGCCTGGGCA 340	1310 ACCGCCCGCCGGG ATCGTCCCCCAGG 350
1320 GACGGC ĠĂĊĂŤCI 360	1330 CCGCGACCGCA CCGAGAACGCA 370	ĠŢĠĠŢĠĂĊĂĂ	1350 GGACCTTCCC GGACCTGCCC 390	1360 CTCGTTGGCCG CTCATTGGC 400	1370 CCCTCAGCGCT	1380 rggccctggtgtg
		TĠĠĂŤĊCGĊC	GCAGCCCCC	AĞCACATCÖT	GGGCCCAGGC	1450 CCAGTTGCTGGCC TCAACTGCTGGCC 470
CCAAGC 480	TĠŦĀĊĊĊĊĀĀĠ 490	CTATACACAG 500	ACATCCACA ATGTGCACA 510	CACĂČĂCACA- CÁCĂCĂCĂCĂCĂT 520	- CACACAC 1 ACACACACCTO 530	1520 FCTCACACACACT GCACTCACACGCT 540
	1540 T-GGAGGGCAA TTGGAGGGCAA 560	GGT-C GGTTCATCAA 570	1550 CACCAGCAC/ CACCAGCATO 580	1560 ATCCACTATCA ATCCACTATCA 590	1570 GTGCTAGACGG GTGCTAAA-TA 600	1580 GCACCGTATCTGC ÀCAGCGAATCTCC 610
1590 AGTGGG ÀÀĜ	1600 CACGGGGGGGC CACTGTGT 620	1610 :CGGCCAGACA ĊĊTĠÄ 63	1620 GGCAGACTGG GGTAGGCAT	1630 GGAGGATGGAG TTGGGG 640	1640 GACGGAGCTGC ĠCĊAAĠĠĊAAĊ	1650 CAGACGAAGGCAG CÁGGTTGGG 660

# FIG.28A

FIG.28B

inputs		0 LLPPLLL(	20 Gafppaaaar		PRQVARLGRT			70 DGRTI
inputs		0 LPOGLKVI		100 1 YVCKATNGF	.10 1 SSLSVNYTLVV			40 QEDPA
inputs		0 TQPSKMRF			180 HPRPDITWMK			210 LSLKN
inputs	22 LRPEDSGKY	-	AGAINATYKV	DVIQRTRSKP	250 VLTGTHPVNT	TVDFGGTTSF	.::	
inputs		GRHNSTI	300 DVGGQKFVVL	310 PTGDVWSRPD	320 GSYLNKLLIT :::::: GSYLNKLLIS 20	330 RARQDDAGMY	340 ICLGANTMG	350 YSFRS
inputs		KPPGPPVA	ASSSSATSLP	WPVVIGIPAG	390 AVFILGTLLL ::::::: AVFILGTVLL 90	WLCQAQKKPC	TPAPAPPLP(	:::::
inputs	**.*.***	KDLPSLA/	ALSAGPGVGL	CEEHGSPAAP	460 QHLLGPGPVA ::.:.: QHILASGSTA 150	GPKLYPKLYT		
inputs	LSCWRARFI 19	: . NTSMSTIS	· ·					

FIG.29

inputs	GT		тетсссстсст	тстсствест	GTGGGCCTGC	GGCTGGCTGG	AACTCTCAAC	CCCA
		10	20	30	40	50	60	70
1 nputs								
		80	90	100	110	120	CACTCCCGCC 130	140
inputs								
•		150	160	170	180	190		210
inputs								
	CAGAGGA	AAACTCCTGG 220	CTTCTAGGGA 230	TTCATTCTGC 240	ATGGTCTGTG 250		AGTGCAGTGG 270	CGAG 280
inputs								
	ATCGTAG	TGCACTGCA 290	ACCTCAAACA 300	GGGAATGCGC 310	TTTCTATGCG 320	CCCTCAGCCC 330	CAGAGTGTTGA 340	GTGG 350
inputs					,			
•		360	370	380	390	400	CAGCGCCTGCA 410	420
inputs								
	TGCCATO	GCTTCTATG 430	AGAGCAGGGG 440	GTTCTGTGTC 450	CCGCTCTGTG 460	CCCAGGAGTO 470	GTGTCCATGGC 480	CGTT 490
inputs								
		500	510	520	530	540	CAGTGCCCCGA 550	560
inputs								<del>-</del>
	CCTTCAG	GCCCTGTACC 570			CTGCCAGTTC 600	CCGCTGCCAGT 610	rgccatggggc 620	ACCC 630
inputs								
	TGCGAT	CCCCAGACTG 640	GAGCCTGCTT 650		GAGAGAACTG 670		GTGACGTGTCC 690	TGTT 700

# FIG.30A

innute							
inputs		TTCTGGCTTCTTC 720				GGTGTCTTCC/ 760	AAACCCC 770
inputs	ACAGGGCTCC	TGCAGCTGCCCCC 790	CTGGCTGGATG	GGCACCATCT	GCTCCCTGC 820	CCTGCCCAGA(	GGCTTT 840
inputs		ACTGCTCCCAGGA/	 Атвт <u>о</u> вство	CACAACGGCGG			GGGCAGT
inputs	850	860	870	880	890	900	910
	GCCGCTGCGC 920	TCCGGGTTACACT( 930	GGGGATCGGT0 940	GCCGGGAGGAG 950	TGCCCGGTG 960	GGCCGCTTTGC 970	GCAGGA 980
inputs	CTGTGCTGAG/	ACGTGCGACTGCGC	CCCCGGACGCC	CCGTTGCTTCC	CGGCCAACG	GCGCATGTCT(	GTGCGAA 1050
inputs	CACGGCTTCAC	CTGGGGACCGCTGC	CACGGATCGCC	CTCTGCCCGA	CGGCTTCTA	CGGTCTCAGC	TGCCAGG 1120
inputs							
	CCCCCTGCACO 1130	CTGĊĠĂĊĊGGGAG( 1140	CACAGCCTCAG 1150 ·	. 1	.0	GAGTGCTCCTC 1180	GCCTGCC 1190
inputs	GGGCTGGGCGC 1200	GGCCTCCACTGCAA 1210	ACGAGAGCTG( 1220		iČGC IČĠĊATGGGC 1240	CAGGGTGCCA 1250	GGAGCAC 1260
inputs	ТСТСТСТССС	TGCACGGTGGCGT0	CTGCCAGGCTA		CTGTCAGTG	CGCGCCGGGT	TACACGG
inputs	1270	1280	1290	1300	1310	1320	1330
	GCCCTCACTG 1340	TGCTAGTCTTTGT0	CCTCCTGACA( 1360	CCTACGGTGTC	CAACTGTTCT	GCACGCTGCT	CATGTGA 1400

FIG.30B

inputs														
	AAATG	CCATCG( 1410	CCTGC	TCACC 1420	CATC	ACGGC 1430	GAGT	3CGTCT 1440	GCAA	GAAGO 1450	STTGG	CAGCGT 1460	GGTAA	CTGC 1470
inputs													<u>.</u>	
	TCTGT	GCCCTG( 1480	CCAC	CCGGA 1490	ACCT	GGGCT 1500	TCAG	TTGCAA 1510	TGCC/	AGCTG0 1520	CAGT	GTGCCO 1530	ATGAG	GCAG 1540
inputs														G
	TCTGC	AGCCCCC 1550	CAAAC	TGGAG 1560	CCTGT	TACCTO 1570	CACC	CCTGGG 1580	TGGC#	ATGGGG 1590	GCCA	CTGCCA 1600	AGCTGC	сст <del>і</del> 1610
inputs	TCCG-												-GTGA	CCCT
·	ŤĊĊĠA	AGGGGCA 1620	\GTTT	GGAGA 1630	AGGTT	TGTGCC 1640	AGTC	GCTGT6 1650	ACTG1	GACCA 1660	CTCT	GATGGO 1670	TĠŤĠĀ	ċċċ† 1680
inputs	30 GTTCA	TGGACAG	40 STGCC	GATGT	50 CAGG	CTGGTT	60 GGAT	GGCAC	70 ACGC	GCCAC	80 CTGC	CTTGC	90 CGGAG	GGCT
•		rĠĠĀĊĠŒ 1690												
inputs	100 TTTGG	GGAGCCA	110 ACTG	CAGTA	120 ACAC	TGTAC	130 CTGC	AAGAAT	140 GGTGG	TACCT	150 GTGT	GTCTGA	160 GAATG	GCAA
		GÄĞTÇA 1760												
innuts	170 CTGCG	reteceo	180 ACCA	GGGTT	190 CCGA	GCCCC	200 TCCT	SCCAĞA	210 GGCCC	TGCCC	220 GCCT	GGTCGC	230	CAAA
Присс		ГĠТĠТĠĊ 1830												
inputs	240 CGCTG	TGTGCA4	250 TGCA	AGTGT	260 AACA	ACAACO	270 ATTC	гтсств	280 CCAC	CATC	290 GACG	GGACCT	300 GCTCC	TGCC
		rĠŢĠĊĊĊ 1900				TÁÁCC		:itċiė						
inputs	310 TGGCG	GCTGG/	320 CAGG	CCCTG	330 ACTGO	TCCGA	340 GGCA	rgtccc	350 CCAG	CCACT	360	ACTCA <i>E</i>	370 ATGCT	CCCA
		GCTGG/												
inputs	380 ACTCT	CCAGTO	390 TCAT	CATGG	400 TGGG/	ACCTGC	410 CACC	CCAGG	420 ATGG	AGCTO	430	TGCACG	440 CCAGG	CTGG
•		CCAATO 204	TĊÁC	ĊÁŤĠĠ	ŤĠĠĠ/	.cctgc	ĊÁTĊ	ĊĊĀĠĠ		ÄĠĊŢĊ		TĠĊĊĊ	ĊŢÁĠĠ	
	<b>∠</b> UJU	204	ͰU	20	วบ	20	160	20	17 U	- 20	uou	21	190	

FIG.30C

- 1070 1080 1090 1100 1110 1120 1130 1nputs CACAGGAATGGCCCAGGACCATTCTGTCATAAAGGTCCCATCTCTGAAGAGGGACTAGGGGCAAGCGTTA -----ÀÀTĠĠĊĊĊÁĠĠĊĊÁŤŤĊŤÁCGÁŤÁÁĠĠĠĊŤĊÁŤĊŤĊŤĠÁÁĠÁĠĠÁĠĊŤĊĠĠĠĠĊĊÁĠŤĠŤĠĠ 2730 2740 2750 2760 2770 2780

FIG.30D

	1140		1150	1160	1170	1180	1190	1200
inputs	TGTCCCT					TGCCCAGCCT		
	:::::	::::::	::::::::	:::::: :::	:::::::::::::::::::::::::::::::::::::::	:::::::::::::::::::::::::::::::::::::::	::::::::	11111111
	CTTCCCT	GAGCAG	TGAGAACCC	ATATGCCACC	ATCCGGGACC	TGCCCAGCTT	GCCAGGGGG	CCCCGGGA
27	790	2800	2810					
	1210		1220	1230		1250	1260	1270
inputs	AAGTGGC	TATGTG	GAGATGAAA	GGACCTCCAT	CAGTGTCCCC	TCCCAGGCAG	TCTCTTCATO	CTCCGGGAC
		:: .:::	::::::::	:: ::::: :	::: ::: :	::::::::	::: :::	: :::::
						CCCCAGGCAG		
28	360	2870	2880	2890	2900	2910	2920	)
	1	280	1290	1300	1010	1000	1000	1040
innute						1320 ACCTATGAGC	1330	1340
mpucs	AGGCAG-	CAGC		AGCCACAGAG		ACCIAIGAGC	AGCCCAGCCC	CITGAGCC
		റ്റാളാളെ				ACCTACGAGC	AGCCCAGCCC	CCTGATCC
20	930	2940	2950					
	. · ·							
	1	350	1360	1370	1380	1390	1400	1410
inputs	ATAATGA	AGAGTCT	TTTGGGCTC	CACGCCCCCG	CTTCCTCCAG	GCCTGCCTCC	TGGTCACTAC	CGACTCCCC
								::::: ::
	::.: .	*** ;:::						
	ATGACCG					GCCTACCCCC		
30		AGACTCT 3010	гатааастс 3020					
30	ATGACCG	3010	3020	3030	3040	3050	3060	) ·
	ATGACCG 000	3010 420	3020 1430	3030 1440	3040 1450	3050 1460	3060 1470	1480
	ATGACCG 000	3010 420	3020 1430	3030 1440	3040 1450	3050	3060 1470	1480
	ATGACCG 000 1 CAAGAAC	3010 420 AGCCATA	3020 1430 ATCCCTGGA	3030 1440 CACTATGACT	3040 1450 TGCCTCCAGT	3050 1460 ACGGCATCCT	3060 1470 CCATCCCCTC	1480 CCATCCCGG
inputs	ATGACCG 000 1 CAAGAAC :::::: CAAGAAC	3010 420 AGCCATA ::::::	3020 1430 ATCCCTGGA ::::::: ATCCCTGGA	3030 1440 CACTATGACT ::::::: CATTATGACT	3040 1450 TGCCTCCAGT :::::::	3050 1460 ACGGCATCCT ::::::: ACGGCATCCC	3060 1470 CCATCCCCTC :::::	1480 CCATCCCGG ::: ::. CCACTTCGA
inputs	ATGACCG 000 1 CAAGAAC	3010 420 AGCCATA	3020 1430 ATCCCTGGA	3030 1440 CACTATGACT ::::::: CATTATGACT	3040 1450 TGCCTCCAGT :::::::	3050 1460 ACGGCATCCT ::::::: ACGGCATCCC	3060 1470 CCATCCCCTC :::::	1480 CCATCCCGG ::: ::. CCACTTCGA
inputs	ATGACCG 000 1 CAAGAAC :::::: CAAGAAC 070	3010 420 AGCCATA ::::::	3020 1430 ATCCCTGGA ::::::: ATCCCTGGA	3030 1440 CACTATGACT ::::::: CATTATGACT	3040 1450 TGCCTCCAGT :::::::	3050 1460 ACGGCATCCT ::::::: ACGGCATCCC	3060 1470 CCATCCCCTC :::::	1480 CCATCCCGG ::: ::. CCACTTCGA
inputs	ATGACCG 000 1 CAAGAAC :::::: CAAGAAC 070	3010 420 AGCCATA :::::: AGCCACA 3080 490	3020 1430 ATCCCTGGA ::::::: ATCCCTGGA	3030 1440 CACTATGACT ::::::: CATTATGACT	3040 1450 TGCCTCCAGT :::::::	3050 1460 ACGGCATCCT ::::::: ACGGCATCCC	3060 1470 CCATCCCCTC :::::	1480 CCATCCCGG ::: ::. CCACTTCGA
inputs 30 inputs	ATGACCG  2000  1 CAAGAAC ::::::: CAAGAAC 270  1 CGCCAGG	3010 420 AGCCATA ::::::::::::::::::::::::::::::::::	3020 1430 ATCCCTGGA ::::::: ATCCCTGGA	3030 1440 CACTATGACT ::::::: CATTATGACT	3040 1450 TGCCTCCAGT :::::::	3050 1460 ACGGCATCCT ::::::: ACGGCATCCC	3060 1470 CCATCCCCTC :::::	1480 CCATCCCGG ::: ::. CCACTTCGA
inputs 30 inputs	ATGACCG  2000  1 CAAGAAC :::::: CAAGAAC 270  1 CGCCAGG	3010 420 AGCCATA ::::::::::::::::::::::::::::::::::	3020 1430 ATCCCTGGA ::::::: ATCCCTGGA	3030 1440 CACTATGACT ::::::: CATTATGACT	3040 1450 TGCCTCCAGT :::::::	3050 1460 ACGGCATCCT ::::::: ACGGCATCCC	3060 1470 CCATCCCCTC :::::	1480 CCATCCCGG ::: ::. CCACTTCGA

FIG.30E

FIG.31A

						ZACCTGGCTG CÁCTTGGCAG CÁCTTGGCAG	
CAGC	2660 GGCGCCT(	2670 GGACGGCTCC	2680 GAGTATGTCA	2690 TGCCAGATO	2700 STCCCTCCGA	2710 GCTACAGTCA ĠĊŤĀTĀĠŤĊĀ 830	2720 CTACTACTCC
		· • • • • • • • •				2780 TAACĀAĢGTTO TAĀCĀĀĢĠŤCO 900	
						0 285 CATGATAACC ĊĠŤĠÅĠÅÅĊĊ 970	
						0 292 GGGGGAGCAG ĠAĠĠĊĠĊĊĀĠ 0 103	
2930	2940	2950		2960	2970	2980	2990
			• • • • • • • • • • • • • • • • • • • •	ŤĠĠĊĊĊĀĠ		CGATAAAGGG TCÁTÁÁÁGGT 90 110	
AAGAG AAGAG 1110	000 GGAGCTCGG GGACTAGG 1120	3010 GGCCAGTGTC GGCAÁGCGT 1130	3020 GCTTCCCTG FÅTGTCCCTG 1140	3030 AGCAGTGA AGCAGTGA 1150	3040 GAACCCATAT GAACCCCTÁT 116	3050 GCCÁCCÁTCC ĠĊTÁĊĊÁŤĊĊ 1170	3060 gggacctgcc gagacctgcc
30	70	3080	3090	3100	3110	3120	3130
						CTCCCTCAGG/ CTCCATCAGT( 0 124(	
						3190 ACAGAGAGACA ÁCÁGÁGGGÁCA 1300	
	* * * * * * * * * *					3260 CCCCCTCTGCC CCCCCGCTTC 1370	

FIG.31B

	3280 ACCCCCCGG	3290 CCACTATGACTO	3300 ACCCAAGAA	3310 CAGCCACATO	3320 CCTGGACATT	3330 ATGACTTGCC	3340 TCCAGTACGG
		TCACTACGACTO 1400 1					
	3350 CATCCCCCA	3360 TCACCTCCACTT	3370 CGACGCCAG	3380 GACCGTTGAG	3390 GGAGCCAGGAT	3400 GGTATGGCAG	3410 AGGCCAGCAC
	1460		.480	1490	1500	1510	
	3420 ACCTGGCTG	3430 TTGCTGCTCAAG	3440 GCTGGGGAC	3450 AGAGCCTAG	3460 TGTACCCCTGC	3470 CAGGAGCAGG	3480 GAGTGGACCG
				1520	1530	1540	1550
	3490 GCAGGCTGT	3500 GAACATGAACAA GAACAGAAACA	3510 CGCTTAACA	3520 GAGCAAGTG .:: .:.	3530 ATGG-GAGCCT	3540 TGTTCCTGGG	3550 -TTCTACCAT
	1560	1570	1580	1590	1600	1610	1620
	3560 GGGAGACGC	3570 TGATCAGCAGGA TAGTTGACAAAG	3580 TGCCTGGCT	3590 CCCTTTCCC :::::::	3600 AACCCACTGCT	3610 CCCAAGGCCT	CCAGGGC
	1630	1640	1650	1660	1670	. 1680	
	3620 CCTGTGT	'ACATAAACTGG1	GGGTTGGAA	GTTGCTGGG	TAAC-TCTGAT	3670 TTTCAGACATG	3680 CGTGTGGGGT
16	90 17	ĠĊĀĠĀĀŤĠŤŦĠŤ 00 1710	172	20 17	30 174	10 175	0
	3690 ACCTTTTCT	3700 GTGC ATGCTC	3710 CAGCCTGGGC	3720 TCTGTGCGT	3730 GTGTGTGTTTC	3740 CTGTGATTTTA	3750 GAAGGGTACC
17		GTGTGTATGCTC					
	3760 AG-GCAGGT	3770 TCTGTCCTAGG	3780 CACTTACCA	3790 TTTAGTAGG	3800 GAGATGGAACO	3810 CAACCCAATTA	3820 ACTCTAGCAA
•		TCTG-CCTTCTC 1840					
	3830 TAGCCTCCT	3840 AACTGGCCTCC	3850 CCATTGATT	3860 CAGTGAACC	3870 TTCCAATGCA	3880 FGGCTCATAAT	3890 TTCAAAATAC
18	90		191	10 19	20	1	930
	AGGCTGGTT	3910 AGTTACTCCCT/	3920 ACCTGAAAGO	3930 CTTCATAGG	TGCCTCTTTG	3950 CTCTTCTGCCA	3960 GTATCAAAAC
	CCÁGTA	ÀTCCTCCATC 1940 19	950	C-TCÁGÁGG 1960		1970	CGACTC
				L-112 'J	-11-		

FIG. 31D

AAAĠĊTĠAAAAAAAAAAAAAAĠĠĠĊĠĠĊĊĠĊ 2540 2550 2560

inputs	MSPPLCPLL	0 LLAVG <b>L</b> RI				50 FSLLPSEPCE		70 PSPQT
inputs			90 GAGVQWRDRS	100 ALQPQTGNAL	110 SMRPQPRVLS	120 GAPSLASPGH	130 TVVVKTDHRO	
inputs			160 QECVHGRCVA	170 PNQCQCVPGW	180 IRGDDCSSAPN	190 CLOPCTPGYY	200 GPACQFRCQC	210 CHGAP
inputs	22 CDPQTGACF					260 PQGSCSCPPG		
inputs	29 HGPNCSQEC	0 RCHNGGLO	300 CDRFTGQCRC	310 APGYTGDRCR	320 EECPVGRFGQ	330 DCAETCDCAP	340 DARCFPANGA	350 CLCE
inputs	36 HGFTGDRCTI	0 DRLCPDGI	370 FYGLSCQAPC	380 TCDREHSLSC	390 HPMNGECSCL	400 PGWAGLHCNE	410 SCPQDTHGPG	420 CQEH
inputs				450 CASLCPPDTY	460 GVNCSARCSC	470 ENAIACSPID	480 GECVCKEGWQ	
inputs	50 SVPCPPGTW	0 GFSCNASO				540 CPKGQFGEGC		
inputs	VHGRCQCQA( VHGQCRCQA( 10	0 GWMGARCH GWMGTRCH 20	580 ILSCPEGLWG ILPCPEGFWG 30	590 VNCSNTCTCK ANCSNTCTCK 40	600 NGGTCLPENG NGGTCVSENG 50	610 NCVCAPGFRG NCVCAPGFRG 60	620 PSCQRSCQPG :::::: PSCQRPCPPG 70	630 RYGK :::: RYGK

# FIG.32A

inputs	RCVPCKCA	.: :: ::::	.::: :::::	:::::::::	:::::: .:.	: :::::::::	
	RCVQCKCN 80	INNHSSCHPS 90	DGTCSCLAGW 100	TGPDCSEAC 110	PPGHWGLKCS 120	QLCQCHHGGTO 130	HPQDGSCICTPGW 140
							760 VMPTTPVAYNSLG
	TGPNCLEG						IMPTSPVTHNSLG 210
	70 AVIGIAVL	780 _GSLVVALVA	790 LFIGYRHWQK	800 GKEHHHLAV	810 AYSSGRLDGS	820 EYVMPDVPPSY	830 SHYYSNPSYHTLS
							SHYYSNPSYHTLS 280
	:::::::	:::::::::::::::::::::::::::::::::::::::	: . : <i>: .</i> : : : :	. :.:.::	:::::::::	::: :::	900 SSRLDRSYSYSYS
	QCSPNPPI 290	PPNKVPGSQL 300	FVSSQAPERF 310	PSRAHGRENH 320	ITTLPADWKHR 330	REPHDRG 340	ASHLDRSYSCSYS 350
inputs							970 SGSAPRQPPQFWD
	HRNGPGPF 360		GLGASVMSLS 380		DLPSLPGEPR		SVSPPRQSLHLRD 420
inputs	980 SQRRRQPO	990 PORDSGTYE	1000 QPSPLIHDRD		1020 PGLPPGHYDS	1030 PKNSHIPGHYD	1040 LPPVRHPPSPPLR
	RQQR QLQ 430	PQRDSGTYE 440		SLGSTPPLP			LPPVRHPPSPPSR 490
inputs							
	RQDR						

FIG.32B

Input file T272Atrxa6b6; Output File T272Atrxa6b6.pat Sequence length 3567

GTCCGAC	CCAC	GCGT	CCGA	GCCA	CACC	CTGA	AGGT	GGTT(	GGAA	GGAG	GGAA(	GGAT	CTAG	GTCC	TGAG	CACTO	GAA	TTCC	79
CCAGAAC	AGCA	TCTG	GCTT	CCCA	GACCO	CATGO	CTGG	CCAC	CACT(	GATG	rgtc(	CTTC	CGCC.	TGCT(	GGCT(	GCAG	rgc to	GTTC	158
TGTTGTT	GGGT	GCCC	TGTG(	GCAG(	CTTO	GTGC/	4ATG(	CCAC.	TCTG <sup>-</sup>	TCCC	CTCC	CCT	CCTG(	CCC.	TAGG(	CCTG(	CGTC	TGGC	237
TGGAACA	CTCA	ACTC	CAAT(	GATCO	CCAA	IGTC'	rgta(	CCTT	CTGG(	GAAA(	CTTO	CACCA	ACGA(	CAC	TAAG(	GAGT	CCA	CCTT	316
CGCCCCT	TCAG	CCTG	CCCC	CAGC	CGAG"	rcct(	GCGA	CAGG	CCCT	GGGA/	AGAC(	CCCC	ACAC	CTGC	GCTC/	AGCC.	FACG(	GTTG	395
TCTACCO	GACT	GTGT	ACCG	TCAG(	GTGG	[GAA(	GATGO	GACTO	CCCG(	CCA	CGCCT	(GCA	STGC	rg tg(	GGGG	TAC	FACG/	AGAG	474
CAGTGGA	GCCT	GTGT	CCCA	CTCTO	STGC	CCAG	GAGT	GTGTO	CCAC	GGTC	CTG	rg tg(	CTC	CTAA'	TCGG	rgcc/	AGTG"	TGCA	553
CCAGGCT	GGCG	GGGT	GACG	ACTG <sup>-</sup>	TTCC	AGTG	AGTG	TGCT	CCTG	GAAT(	GTGG(	GAC	CACA	GTGT	GACA	GCT	CTGC	CTCT	632
GTGGCAA	CAGC	AGTT	CCTG	TGAT	CCCA	GAG	TGGG	GTGT(	GTTT	TTGC	CCCTO	CTGG	CCTG	CAGC	CCCC	CGAC	rgcc°	TTCA	711
GCCTTGC	CCCG	ATGG	CCAC	TATGO	GTCC	rgcc:	TGCC	AGTT	TGAT	TGCC	ATTG(	CTAT	GGGG	CATC	CTGTO	GACC	CCCG	GGAT	790
GGAGCCT	GCTT	CTGC	CCCC	CAGG	GAGA	ACAG	GACC	CAGG	GCAC	TGAT	GCT	ICTT(	CTGC	CCCA	GAAC'	TAT	CCTT	GCCA	869
AAATGGA	GGTG	TTCC	TCAG	GGCT(	CTCA	AGGC.	TCCT	GCAG	CTGC	CCAC	CGGG	CTGG	M ATG	G GGT	V GTC	I ATC	•	•	6 942
L P	C TGC	P CCA	E GAG	-	F TTC	H CAC	G GGA	P CCC			T ACT	Q CAG	.E Gaa	C TGT	R CGT	C TGC	H CAC	N AAT	26 1002
						-	^	^	С	н	С	Α	р	G	γ	1	G	D	
G G GGT GGC	L CTT	C TGT	D GAC	R AGG	F TTT	T ACT	G GGG	Q CAG	-					_	-	•	•		46 1062
	CTT R	TGT E	GAC E	AGG C	TTT P	ACT V	GGG G	CAG R	TGC F	CAC G	TGT Q	GCT D	CCT	GGC A	TAT	ATC T	GGG C	GAT	

# FIG.33A

TERLCPD TGDR C GRYGLS 106 ACA GGC GAC CGC TGC ACT GAG CGA CTC TGT CCA GAT GGC CGC TAT GGT CTG AGC TGC CAA 1242 D P E H S L S СНР 126 M H G GAT CCC TGC ACC TGC GAC CCA GAA CAC AGT CTC AGC TGC CAC CCA ATG CAC GGC GAG TGC 1302 Q P A G L H C Ε S C N 146 TCC TGC CAG CCA GGT TGG GCG GGC CTC CAC TGC AAC GAG AGC TGC CCT CAG GAC ACG CAC 1362 GAGCQE H C L C L H G G V C 166 GGA GCC GGT TGC CAG GAG CAC TGC CTC TGT CTG CAC GGC GGT GTT TGC CTC GCC GAC AGC 1422 R C Α P G Y TGPH 186 C N Α GGC CTC TGC CGG TGT GCA CCT GGC TAC ACG GGA CCT CAC TGC GCT AAT CTT TGT CCA CCT 1482 Y G 1 N C S S H C S C E N A I A 206 AAC ACT TAT GGG ATC AAC TGT TCC TCC CAC TGC TCC TGT GAA AAT GCC ATT GCC TGC TCT 1542 P V D G T C ICKEGW C S 226 QRG N CCT GTC GAC GGC ACG TGC ATC TGC AAG GAA GGT TGG CAG CGT GGT AAC TGC TCT GTG CCC 1602 G F S C N A S C Q C A H Ε 246 TGT CCC CCT GGC ACC TGG GGC TTC AGT TGC AAT GCC AGT TGC CAG TGT GCC CAC GAG GGA 1662 Ţ G A C T C T Р G W R ٧ 266 GTC TGC AGC CCC CAA ACT GGA GCC TGT ACT TGC ACC CCT GGG TGG CGT GGG GTT CAC TGC 1722 K G Q F G E G C A S ٧ 286 CAA CTT CCG TGC CCG AAG GGA CAG TTT GGT GAA GGT TGT GCC AGT GTC TGT GAC TGT GAC 1782 D PV Н G H C R C Q 306 CAC TCC GAT GGC TGT GAC CCT GTT CAT GGA CAC TGC CGA TGT CAG GCT GGC TGG ATG GGC 1842 PCPEGFWG C 326 Α N ACA CGT TGC CAC CTG CCT TGC CCA GAG GGC TTT TGG GGA GCC AAC TGC AGC AAT GCC TGT 1902 G T C V P E N C V C N G 346 ACC TGC AAG AAT GGT GGC ACT TGT GTA CCT GAG AAC GGC AAC TGT GTG TGC GCA CCA GGG 1962

## FIG.33B

R G P S C Q R P C P P RYGKRCV 366 G TTC AGA GGC CCC TCC TGC CAG AGG CCC TGC CCG CCT GGT CGC TAT GGC AAA CGC TGT GTG 2022 NNHS S C H P S 386 0 G Ţ CCC TGC AAG TGC AAC AAC CAT TCT TCC TGC CAC CCG TCG GAT GGG ACC TGC TCC TGC CTG 2082 TGP D C S E S C Ρ Ρ G 406 GCA GGC TGG ACA GGC CCT GAC TGC TCT GAA TCA TGT CCC CCA GGC CAC TGG GGA CTC AAA 2142 426 Q C H H G A T C H P Q TGC TCC CAA CCC TGC CAG TGT CAT CAT GGT GCC ACC TGC CAC CCC CAG GAT GGG AGC TGT 2202 Р SE C P 446 G N С G GTC TGC ATC CCA GGC TGG ACT GGA CCC AAC TGC TCG GAA GGC TGC CCA TCA AGA ATG TTT 2262 C SQLC QCD PGEMC Ε 466 CGT GTC AAC TGC TCC CAG CTA TGT CAG TGT GAT CCT GGA GAG ATG TGC CAC CCA GAG ACT 486 GACVCPPG H S G AHCKVGS GGG GCT TGC GTC TGT CCC CCA GGA CAC AGT GGT GGG CAC TGC AAA GTG GGC AGC CAG GAG 2382 506 1 M P T S P V 1 H N S L G A V TCC TTC ACC ATA ATG CCC ACC TCT CCT GTG ATC CAT AAC TCA CTG GGT GCC GTG ATT GGC 2442 ٧ VALF 526 ٧ Α L ATT GCA GTG CTG GGG ACC CTT GTG GTG GCC CTG GTA GCA CTG TTT ATT GGC TAC CGA CAC 2502 546 É H E H L ΑV A Y S TGG CAA AAG GGC AAG GAA CAT GAG CAC TTG GCA GTG GCT TAC AGC ACT GGG CGA CTG GAT 2562 YVMPDVSPSYSHYY 566 GGC TCC GAT TAC GTC ATG CCA GAT GTC TCT CCG AGC TAC AGT CAC TAC TAT TCC AAC CCT 2622 586 S Q C S PNPPP AGC TAC CAC ACA CTG TCT CAG TGT TCT CCT AAC CCT CCA CCC CCT AAC AAG ATT CCA GGC 2682 V S S Q A S ERPN R N H G 606 AGT CAG CTG TTT GTC AGC TCC CAG GCA TCT GAG CGG CCA AAC AGA AAC CAT GGG CGA GAT

# FIG.33C

N AAC			T ACA				D GAC			H CAC			E GAG	_	H CAT	D GAC	R AGA	A GCT	F TTC	626 2802
_	R AGG	H CAC	Q CAG	P CCA	P CCT	G GGA	P CCG	K AAG	V GTA	* TAG										637 2835
CTG	[AGC]	TATGO	GCCA	CAGGA	AATG(	GCCC(	GGGG	CCAT	rctg <sup>-</sup>	TCAT	AAAG(	STCCC	CATC	rctg/	\AGA/	AGGA(	CTAG(	GGCA	AGC	2914
GTT	ATGT(	CCCT	GAGC	AGTG/	AGAA	cccc	TATGO	CGAC	CATC	CGAG	ACCT(	GCCCC	GCC	TGCC'	rggg(	GAAC	CCCG	AGAAA	AGCA	2993
GCT	ATGT(	GGAG	ATGA	AAGG(	CCT	CCAT	CAGTO	STCTO	CCCC	CCAG	GCAG(	CTC1	TTCA	rctc(	DGGG/	ACAG(	GCAG(	CAGC	AGCA	3072
ACT(	CAGT	rctc/	AGAGA	AGACA	AGCG(	CAC	CTATO	SAGC/	AGCC(	CACTO	CCCTT	GAGC	CCGTA	\ATG/	NAGA(	STCTO	GTGGG	CTC	CATG	3151
CCC	CTCT	TCCT	rccg(	GCCT	rgcc/	ACCCC	GCC/	CTA	[GAC]	TCGC(	CAAA	\AAC <i>A</i>	AGCC/	CATO	CCTC	GGACA	ACTA	GACT	TGC	3230
CTC	CAGTA	ACGG(	CATCO	CTCCA	ATCAC	CCTC	CATCO	CGG(	CCCA	AGGA(	CCGC1	GAGO	AGCC	CAGCA	ATGGT	TATG(	GAG/	GTGC	CTG	3309
TGAA	CCC1	rgcc/	AGGAC	CAGO	GCC	GGA(	CAGC	AGG(	CATO	SAATA	AGAC#	TACT	TGGT	GAAG	TGAA	ACGG/	AGAC1	GAGG	ATG	3388
GCT(	CTGCT	TCCA	ACCG/	AGGG/	\GAC/	ACTA(	STTGO	CAA	AGTG1	TCTA/	ACCTO	CCTT	TTC	CAGCO	CAT	FGC10	CAAGT	rcccc	CAG	3467
GCT(	TGGA	CATO	GAGC	rgg t (	GGC/	\GAA1	GTTG	STTGT	TGA	AGTC	[GAT]	TTAG	SATTO	SATT1	TTT	\AAA/	\AAA/	\AAA/	AAA	3546
AAAA	AAAA	\AAA(	GGCC	GCCC	C						•									3567

FIG.33D

69/95 GTC-GACCCACGCGTCCGCAAGCGGGGACCCTCGCCCCGTCCTCGGCTGTCCAGTCCTCCTCGC ... ............. ::: :::::: :. GTCCGACCCACGCGTCCG----AGC----CACACCCTGAAGGTGGTTGGAAGG--rat ... :::::...:: :.::. . ::: ..: ---GAAGGATCTAGGTCCTGAGCACTGG-----AATTCCCCAGAACAG-CATCTGGCTTCCCAGA rat CGCTGG-GATCCCCCA-GGACATTCCCTGGCCCCCAGGCCCCAGGCCCCAGGCCCCAGGCCTGAGCTGTG human : :. : . :: ::: :: :: ::: : . : CCCATGCTGGCCACCACTGATGTGTCCTT----CCGG-- CTGGCTGCAGTGCTGTTCTGTT rat CTG--GGCAGGCCCCACCTGGCCTCTGCAATGTCACCGCCTCTGTGTCCCCTCCTTCTCCTGGCTGTGGGCCTGC human GTTGGGTGCCCTGTGGCA--GGCTTGTGCAATGCCACTCTGTCCCCTCCTCCTGGCCCTAGGCCTGC rat GGCTGGCTGGAACTCTCAACCCCAGTGATCCCAATACCTGCAGCTTCTGGGAAAGCTTCACTACCACCAC human GTCTGGCTGGAACACTCAACTCCAATGATCCCAATGTCTGTACCTTCTGGGAAAGCTTCACCACGACCAC rat CAAGGAGTCCCACTCCCGCCCCTTCAGCCTGCTCCCCTCAGAGCCCTGCGAGCGGCCCTGGGAGGGCCCC TAAGGAGTCCCACCTTCGCCCCTTCAGCCTGCCCCCAGCCGAGTCCTGCGACAGGCCCTGGGAAGACCCC rat CATACTTGC-CCCAGCCCACAAA---CT--CAGA---GGAAACTCCTGGCT-TCTAGGGATTCATTCTGC human :: :: ::: : ::::: ::... :: :.:: :.: : :.:: 1 .::. . .:. CACACCTGCGCTCAGCCTACGGTTGTCTACCGGACTGTGTACCGTCAGGTGGTGAAGATGGACTCCCGCC rat ATGGTCTGTGTCGGGGCTG-GAGTGCAGTGGCGAGATC-GTAGTGCACCTCAAACAGGGAATGC human CACGCCTG---CAGTGCTGTGGGGGTTACTACGAGAGCAGTGGAGC-CTGTGTCC-CACTCTG----TGC rat GCTTTCTATGCGCCCTCAGCCCAGAGTGTTGAGTGGTGCCCCTTCCCTG-GCCTCCCCTGGCCACACTGT human CCAGG-AGTGTGCCACGGTC-----GCTGTGTG--GCTCCTAATCGGTGCCAGTGTGCACCAGGCTGG rat 

### FIG.34A

FIG.34B

									71/	95									
human	TÇ	GCCTC	TGC(	CCCG	ACG(	CTTC	TAC	GGT(	L340 CTCAG	CTGC	CAGG	CCCC	CTG(	CACC	TGC	GAC	CGGG/	\GCA	CAGC
rat	GC	GACTC 121	.0		1220	)	. 1	230		124	0	1	250		1	L260	ĊĊĂĠĀ		CAGT 270
human	CT		GCC	ACCC	GAT	BAACG	iggg	AGT(		TGCC	TGCC	GGGC	TGG	GCGG	GCC	CTCC			
rat	ĊŤ	CAGCT 128	GCC.	accc	AAT( 129(	GCACG	igcg	AGT(	CTCC	TGCC	AGCC/	aggt	TGG(	GCGG	iGCC	TCC 1330	actgo	134	GAGA
human	GC	TGCCC	GCA	GGAC	ACG	CATGG	igcc	AGG(	GTGCC	agga	(GCAC	TGTC	TCT	GCCT	GC/	\CGG	TGGC	тст	GCCA
rat	GC	TGCCC 135	TCA 0	GGAC	ACG( 136(	ACGG )	AGC	CGG 370	riccc	AGGA 138	GCAC	TGCC 1	TCT( .390	arct	GCA	CGG L400	CGGT	14	GCCT 10
human	GG	CTACC	AGC	GGCC	TCT(	GTCAG	TGC	GCG	CCGGG	TTAC	ACGG	GCCC	TCA	CTGT	[GC]	ragt	CTTTC	GTCC	тсст
rat	CG	CCGAC 142	AGC O	GGCC	TCT( 143(	accge )	TGT 1	GCA( .440	CCTGG	CTAC 145	ACGG 0	GACC 1	TCA 460	CTGC	GCT:	ГААТ 1470	citio	STCC	ACCT 180
h≀man	ı GA	CACCT	ACG	GTGT	CAA0	TGT	CTC	CAC	GCTGC	LCAT	GIGA	AAAI	GCC	ATCO	iCC	I GC I	1650 CACC(	CATO	GACG
rat	ÁĀ	CACT 1 149	ATG 0	: .: GGAT	CAA 150	CTGTT	CCT 1	CCC .510	ACTGC	:: : TCCT 152	GTGA 10	AAAT 1	GCC. .530	ATTO	CC	rgct 1540	ctcc	rĠTC 15	GACG 550
human	1660 GC	GAGTO	CGT	CTGC	AAG	GAAGG	TTE	GCA	1690 GCGTG	<b>GTAA</b>	CTGC	TCTG	TGC	CCTG	acco	CACC	CGGA/	ACCT	GGGG
rat	GC	ACGTO	CAT 0	CTGC	::: AAG 157	GAAGG O	::: TTG 1	GCA .580	GCGTG	GTAA 159	CTGC 0	:::: TCTG 1	TGC .600	CCTG	TC	CCCC 1610	TGGC	ACCT 16	GGGG S20
human	1730 CT	TCAGT	17 TGC	AATO	CCA	GCTGC	CAG	TGT	GCCCA	TGAG	GCAG	TCTG	icag	CCCC	CA	4act	GGAG	CCTO	STACC
rat	ĊŤ	TCAGT 163	TGC 80	<b>AAT</b> 0	CCA 164	GTTGC	CAG	TGT	GCCCA	CGAG	GGAG	TCTG	icag	CCCC	CA	4act	GGAG	CCTG	TACT 90
human	1800 TG	CACCO	18 CTG	GGT	GCA.	TGGGG	CCC	ACT	GCCAG	CTGC	CCTG	TCCG	aag	GGGC	CAG	TTTG	1860 GAGA	AGG1	тстс
rat	TG	CACCO	CTG	GGT	GCG	TGGGG	TTC	ACT	GCCAA	CTTC	CGTG	CCCG	aaag	GGAC	CAC	TTTG	GTGA	AGGT	TGTG 760
human	1870 1 CC	AGTCG	18 CTG	80 TGAC	TGT	1890 GACC <i>A</i>	) NCTO	TGA	1900 TGGCT	GTGA	191 CCCT			1920 GAC		<b>ETCA</b>	1930 GTGC(	CAGO	CTGG
rat	ċċ	AGTGT 177		TGAC	TGT 178			CGA 1790		GTGA 180		GTTC 1	ATG L810	GAC/	ACT	: :. GCCG 1820	ÁŤĠŦ	CAG0	CTGG 330
humar	1940 CT		19 GGT	50 GCC0	CGCT	1960 GCCA0	) CTO	STCC	1970 TGCCC	TGAG	198 GGCT	O TATO		1990 AGT0			2000 AGCA	4CA(	CCTGC
rat	::	GGATO	GGC	.: :	: :	GCCAC	CTO	: :	TGCCC	. : : :	GGCT	: : : : 1110	::::	AGC	::: CAA	:::	ÁGCÁ	: ATG	::::

FIG.34C

			70	/OE			
2 human	ACCTGCAAGAATG	2030 GGGGCACCTG	2040 FCTCCCTGAG	BAATGGCAACT	GCGTGTGTGC	ACCCGGATTC	CGGGGCC
rat	ACCTGCAAGAATG	GTGGCACTTG 1920	GTACCTGAG	AACGGCAACT	GTGTGTGCGC	ACCAGGGTT	AGAGGCC
2 human	.080 2090 CCTCCTGCCAGAG	2100 ATCCTGTCAG	2110 CCTGGCCGCT	2120 ATGGCAAACG	2130 CTGTGTGCCC	2140 TGCAAGTGCG	CTAACCA
rat	-::::::::::::::::::::::::::::::::::::::	GCCCTGCCCG	CTGGTCGCT	ATGGCAAACG	:::::::::	TGCAAGTGCA	
2	150 2160	2170	2180	2190	2200	2210	
numan	CTCCTTCTGCCAC	CCCTCGAACGC	GACCIGCIA	CTGCCTGGCT	GGCTGGACAG	GCCCCGACTG	CTCCCAG
	2050	2060	2070	2080	2090	2100	2110
2 human		GACACTGGGG/	AGAAAACTGT	GCCCAGACCT	GCCAATGTCA	CCATGGTGGG	ACCTGCC
rat		CCACTGGGGA	CTCAAATGCT	CCCAACCCTG	CCAGTGTCAT	CATGGTGCCA	CCTGCC
2	290 2300	2310	2320	2330	2340	2350	•
	ATCCCCAGGATGG	::::::::::::	::: :: ::	::::::::::::	:: : :::::	: .:::::::	::::.
rat		2200	2210	GCTGGACTGG 2220	ACCCAACTGC 2230	TCGGAAGGCT 2240	GCCCATC 2250
2 human	360 2370 GGGGACATTTGGT	2380 GCTAACTGCT(	2390 CCAGCCATG	2400 CCAGTGTGGT	2410 CCTGGAGAAA	2420 AGTGCCACCC	AGAGACT
rat		GTCAACTGCTC	CCAGCTATG	TCAGTGTGAT	CCTGGAGAGA	TGTGCCACCC	AGAGACT
2	2260 430 2440	2450	2460	2470	2480	2490	
human	GGGGCCTGTGTAT	GTCCCCCAGG@	GCACAGTGGT	GCACCTTGCA ::::	GGATTGGAAT	CCAGGAGCCC	:: :: .
rat		GTCCCCCAGG/ 2340	ACACAGTGGT 2350	GCGCACTGCA 2360	AAGTGGGCAG 2370	CCAGGAGTCC 2380	TTCACCA 2390
2 human	500 2510 TGATGCCGACCAC	2520 TCCAGTAGCGT	2530 TATAACTCGC	2540 TGGGTGCAGT	2550 GATTGGCATT	2560 GCAGTGCTGG	GGTCCCT
rat	TAATGCCCACCTC	 TCCTGTGATCO	ATAACTCAC	TGGGTGCCGT	GATTGGCATT	GCAGTGCTGG	::::::
2	2400 570 2580	2410 2590	2420 2600	2430	2440	2450 2630	2460
human	TGTGGTAGCCCTG	GTGGCACTGTT	CATTGGCTA	TCGGCACTGG	CAAAAAGGCA	AGGAGČACCA	CCACCTG
rat	TGTGGTGGCCCTG 2470		TATTGGCTA 2490	CCGACACTGG 2500	CAAAAGGGCA 2510	AGGAACATGA 2520	GCACTTG 2530
2 human	640 2650 GCTGTGGCTTACA	2660	2670		2690 TCATGCCAGA		۸۵۳۳۸۵۸
rat	GCAGTGGCTTACA	:: :::::	:::: ::::	::::: :: :	::::::::::	:::: :::::	::::::
- -	2540		2560	2570		2590	2600

FIG.34E

rat	ĠĠĠĀĠ 3300	j=			· ÀĠ	iŤĠĊĊŤ-ĠŤĠĂ 3310	3460 ACCCCTGCCAGGA ÁCCC-TGCCÁGGÁ 3320
human rat	3470 GCAGGGA GCAGGGC 3330	3480 GTGGACCGGC CTĠĠĀĊĊĀĠĊ 3340	3490 AGGCTGTGAA ÀĠĠĊ	3500 CATGAACAAC ĊĀŤĠĀĀ 3350	3510 GCTTAACAGA ŤÁĠÁĊÁTÁ	3520 GCAAGTGATG	3530 GGAGCCTTGTTCC
human rat	3540	3550 TACCATGGG/	3560 AGACGCTGATC	3570	3580	3590 TTCCCAACCC	3600
human rat							3670 TTCAGACATGCGT
human rat	3680 GTGGGGT	3690 ACCTTTTCTG	3700 TGCATGCTCA ĊTĊT 3390	3710 GCCTGGGCTC ĠĊ	3720 TGTGCGTGTG	3730 TGTGTTTCTG	3740 TGATTTTAGAAGG
human rat	3750 GTACCAG - ††ĊĊĀ - 3400	3760 GCAGGTTCTG	3770 TCCTAGGGCA - CCGAGGG	3780 CTTACCATTT	3790 AGTAGGGAGA	3800 TGGAACCAAC	3810 CCAATTAACTCTA ÀĠÁĊÁĊŤÁ 3410
human rat						3870 AATGCATGGC ††ĠĠĊ 3420	3880 TCATAATTTCAAA
human rat						3940 TCTTTGCTCT	3950 TCTGCCAGTATCA
human rat							4020 CACCTTGAACTGT
human rat	4030 GTTCCTG						4090 TCTTTCTGGCACA

FIG.34F

human rat		4110 TGCACACCT				4150 CCACCCCTGCT :: ::: 3440	4160 TITCCTTTACACCTC
human rat	4170 CTCCTC.		4190 CCCACCCTCC	4200 GTACATCTTT	4210 CACAGCCCTC	4220 GATTGCAGCTG	4230 IGTTCACTCACCAGG ĊÅÅĠ
	4240 TACCTG † 460		4260 TACAGGGTGC			4290 TCTTTCTTTA	4300 FGTGATTATTTGATT
human rat			• •			4360 ATCCTGTGCT	4370 FATGCTCAATATTAG
human rat							4440 CTGACTGAATTAAGT
		4460 GACATGCAG GACATG		4480 GATAGATGAG		4500 GCTCTGACAGT	4510 TTACAGACTGAATAA
human rat	4520 GTTGGA	4530 GACTTCCCT	4540 AAAGGGTGGC/	4550 ATTTCCCCAG	4560 GGTAACAACG	4570 CAGAGCTCAGG	4580 GTGTGGGAAGGTGCC
human rat	4590 AGGGGC	4600 AGGGGTGCA	4610 GAGGGGCTGAG	4620 GGCTGAGGGG	4630 GGTGCAGAGG ÀĠ 3480	4640 CTGGAGAAAGO CTGGTGG	4650 GATAACAGGAGAGAG
human rat	4660 TATACA	4670 GCATGCCT	4680 TGATTTATTGO	4690 CACTTCACAG	4700 GTAGCAGAAT	4710	4720 ATTGAAGGTTTTGGG
human rat							4790 STGTCAACACTGCTT

# FIG.34G



FIG.34H

	GTCCGAC	CACGCGT 10	FCCGG1 :::: FCCGAGCC <i>I</i> 20	GACCCTGTT :::::: ACACCCTGA/ 30	AGGTGGTTGGAA( 40	GCCGATG : : : : : : : : : : : : : : : : : : :	TCAGGCTGGT ::::: TCTAGGTCCTGAGCAC 60 70
inputs	TGGAATTO	CCCAGA/ 80	ACAGCATCT 90	rggcttccc/ 100	AGACCCATGCTG 110	GCCACCACTGA 120	110 GGAG-CCAAC-TGCAG :.: :: ::: TGTGTCCTTCCGGCTG 130 140
	-TAACACC CTGGCTGC	AGTGCTO 50	TGCAAGAA : : TTCTGTTG 160	ATGGTGGTAC : : : : GTTGGGTGCC 170	CTGTGGCAGGC 180	T-GAGAATGGCA : ::: :: TTGTGCAATGC0 190	
inputs	стсстсст	GTTCCG/ : :::: GGCCCT/	NGGCCC - CT ::::: NGGCCTGCG	CCTGCCAGA :::::::::::::::::::::::::::::::::	: :: ::	CC TGGTCGCT CCAATGATCCC/	230 FATGGCAA-ACGCT LIII III III AATGTCTGTACCTTCT 270
inputs	: :. :: GGGAAAGC 280	TTCACCA 290	ACGACCACT 300	AAGGAGTCO 310	-AACAACAACCA : ::. :: CACCTTCGCCCC 320	CTTCAGCCTGCC 330	CACCCATCG : :: :: :: CCCCAGCCGAGTCCTG 340
inputs inputs	GTGTGC :::::::::::::::::::::::::::::::::::	AATGC 290  CCTG : : : : : : : : : : : : : : : :	ACGACCACT 300 300 300 CTCC : :: AGGACCCCC 370	TAAGGAGTCC 310 310 T-GCCTG CACACCTGCG	-AACAACAACCA :::::::::::::::::::::::::::	ATTCTTCCTGCC  III. IIIIII CTTCAGCCTGCC  330  320  ACAGGC CCTG  IIIII GTTGTCTACCGG  400	CACCCATCG  CCCCAGCCGAGTCCTG 340  330  GACTGCTCCGAG  CACTGTGTACCGTCAG 410
inputs inputs	GTGTGC :::::::::::::::::::::::::::::::::::	CCTG CCTGGGA 360  440 -ATG GATGGAC	300 300 300 CTCC :::: AGACCCCC 370 -TCCCCC	TAAGGAGTCC 310 310 CT-GCCTG CACACCTGCG 380 380 CAGGCCA CACGCCTGCA	-AACAACAACCA :::::::::::::::::::::::::::	ATTCTTCCTGCC  III III III III III III III III III	CACCCATCG  CCCCAGCCGAGTCCTG 340  330  GACTGCTCCGAG  CCCCAGCGAGTCCTG 410  370  GCTCC

# FIG.35A

				10155			
inputs	420 CAGGATGG	GAGCTGT	430 TATC	TGCÀCGCCA	0 450 GGCTGGACTG	) GACC-CAA	460 CTGC GACAGGCTCTGC
	560	5/0	580	590	600	910	620
inputs	TTGGAAGG	70 CTGC	CCA	480 CCAAGAATG	490 TTTGGTGT		-CAACTGCTCC
	630	640	650	000	670	680	690
inputs	C	· AGCTATO	TC - AGTG-	TGA CCACTAŤĠĠ	TCTC	GGAGAGATG	····TGC·····
	700	710	720	/30	/40	/50	760 580 GTGGTG
inputs	GGCATCCTC	TGACCCCCGG	GATGGAGCC	TGCTTCTGC	CCCCCAGGGA	· · · · · · · ACACA :: :: BAACAGGACCCA 820	GGGCACTGATG
inputs	CA(						620 CACCATAA- AGGCTCCTGCAG
•	GCTTCTTC	: TGCCCCAGAA( 850	TTATCCTTG 860	CCAAAATGG 870	ÄĠĠŢĠŢŢĊĊŢŒ 880	CÁGGGCTCTCÁA 890	AGGCTCCTGCAG 900
inputs	-TGCCCAC	)	630 TC:	TCCCG-	640 TGACCCATA	AACTC-	650 ACTGG GGACCCAACTGT
	910	920	930	940	950	900	970
inputs	660 GTGCAGTG/	670 ATTGGCATTG	680 CAGTACTGGG	690 AACCCTCGT	GGTGGC	700 CCTGATAGC	710 CACTGTTCAT-T
	980	990	1000	1010	1020	1030	1040
inputs	GGCTA	CEGEGATCEGT	CCG	CCAG	730 TGG TGGGCCGCTT(	CAAAAG	740 GGGCAAGGAACA TGCTGAGACCT
	1050	T000	T0\0	1080	1090	TTOO	TTTO
inputs	GTGACTGT	GCACTTGGCA GCTCCTGGCG	GTGGCTT CTCGTTGCTT	AC TCCTGCCAA	-AGCACTGGĠĠ TĠĠĊĠĊGTĠTŒ	CGGCTGG-AT	790 FGGCTCTGATTA FGGCTTCÁCÁGG
	1120	1130	1140	1150	1160	1170	1180

# FIG.35B

inputs	800 CGTCATG CGACCGCTG 1190	810 GC-CAGAT-GT SCACTGAGCG/ 1200	820 FCTCTCCG/ CTCTGTCCA( 1210	AGCT ::: GATGGCCGCT 1220	830 ATAGTCACTA ATGGTCTGAG 1230	840 ACTACT GCTGCCAAGAT 1240	850 -CCAACCCCAGC CCCTGCACCTGC 1250			
inputs	TACCACA GACCCAGAA 1260	860 ACACTGTCTC/ ACACAGTCTC/ 1270		880 FAACCGCCCG	890 CCCCC CGAGTGCTCC	TAACA AC	900 GGTCCCAGGCA			
1:	TCCÁCTĠĊÁ 330	920 - CTTTGTCAG AACGAGAGCTG 1340	930 GCCCTCAGGCC GCCCTCAGGAC 1350	94 C-CCTGA CACGCACGGA 1360	0 GCGGCC :: ::: GCCGGTTGCC 1370	950 AAGCAGAG : :::: AGGAGCACTG 1380	GCCCA :: CCTCTGTCTGCA 1390			
•	1400	1410	1420	1700	7-1-10	1-750				
inputs	1020 ATGACAGAG TAATCTTTG 1470	1030 GGC-GCCAGCC TCCACCTAAC 1480	CAC CACTTATGGGA 1490	10 CTGGA ATCAACTGTT 1500	40 1 CCGAA-GCTA CCTCCCACTG 1510	.050 TAGCTGTA CTCCTGTGAA 1520	1060 GCTATAGCC AATGCCATTGCC 1530			
inputs	ACA †GCTCTCCi 1540	1070 AGG-AATGGCO GTCGACGGCA 1550	1080 CCAGGAC ACGTGCATCTG 1560	CATTGCAAGGAAGG	1090 CTGTCATAAA TTGGCAGCGT 1580	1100 GGTCCCATCT GGTAACTGCT 1590	1110 CTGAAGA- CTGTGCCCTGTC 1600			
inputs	CCCCTGGC	ccteeecti	130 AGCGTTA-TGT CAGTTGCÁAT 1630	GCCAGTTGC	cA-ĠŤĠŤĠĊĊ	CACGAGGGAG	1160 TGCTACC TCTGCAGCCCCC 1670			
inputs	1170 -ATCCGAGA AAACTGGAG 1680	ACCTG CCTGTACTTG 1690	180 CCCAGCC GCACCCCTGGG 1700	1190 TGCC-TGGGG TGGCGTGGG 1710	GAACCO GTTCACTGCC 1720	1200 CGAG :::: AACTTCCGTG 1730	1210 iAAAGTGGCT i::::::::::::::::::::::::::::::::::::			
inputs	ATGTGGAGA GTTTGGTGA 1750	1230 TGAAAGGACO AGGTTGTGCO 1760	CAGTGTCTGTG 1770	ACTGTGACC	1250 CCTCCCA-GG ACTCCGATGG 1790	CAGT CT CTGTGACCCT 1800	60 CTTCATC :::::: GTTCATGGACAC 1810			
	FIG.35C									

inputs	1270 T-CCGG-GACA TGCCGATGTCA	1280 AGGCAG-CAG-		1290 CGGCAAC	D 1 TGCAGCCA	300 CAGAGGG A	1310 CAGCGGCACC
	TOLU	1000	70-40	1000	1000	10/0	1990
inputs	1320 TA-TG-AGCA AACTGCAGCAA	GCC	.330 :AGC	·CCCTT(	1340 GAGCCATA	1350 ATGAAGAGTC	TTTGGG
	1890	1900	1910	1920	1930	1940	igigigigigigi 1950
130 inputs	CTCCA	137 CGCCCCC	CCTTCCTCC	\GGCCTGCC_7	TCCTGGTC &C	TACGACTC.	CC
		1970	1980	1990	2000	2010	2020
14: inputs	10 CCAAGA CTGCAAGTGCA	1420 NACAGCCATA	1430 TCCCTG	GAC	1440 ACTATGA	CTTGCCTC	1450 CAGTAC-
	2030	2040	2050	2000	2070	2080	2090
inputs	1460 GGCATC	·CTCCA	1470 TCCCCT-	-CCA	· · · · · · · · · · · · · · · · · · · ·	1480 -TCCCGGC	-GCCAG-GAC
	2100	CICIGAATCA 2110	AGTCCCCCAG 2120	GCCACTGGGG 2130	ACTCAAATG 2140	CTCCCAACCC 2150	TGCCAGTGTC 2160
149 inputs	OO 15 CGC-TGAAGA- ATCATGGTGCC	500 -GCCGGCAT	1510 GGTATGG	1520 GAGC - GTGCC	1530 CTATGTACCT	TGC CAG	1540 GAG
	21/0	ZTO0	<b>7130</b>	2200	2210	2220	2230
inputs	CAGGGACTG-	50 ·GACCAGCAGG	1	.560 CCACG	1570 AACAGA	4ACA	1580 CTTGGTGAA
	CTCGGAAGGCT 2240	rgcccatgaag 2250	AATGTTTGGT	GTĊAÄĊTGCT	rcccágctát 2280	GTCAGTGTCAT	rcctggagag 2300
inputs	GTGAAC ATGTGCCACCC	01600 1610 AGAGACGGAC	1620 16 TGTGGC-CCT	30 GTGCTTC	-CACCGAGG	GAGACACT	- AGTTGACA
	ATGTGCCACCC 2310	ÄĞÄĞÄCTĞĞG 2320	GCTTGCGTCT 2330	GTCCCCCAGG 2340	ACACAGTGG 2350	TĠĊĠĊĂĊŤĠĊ <i>A</i> 2360	AAGTGGGCA 2370
inputs	1640 1 AAGTGTCT	L650 TAAC-CCTCTT	1660 TTCCAACC-C	1670 ACTGCTC	168 AAGTCC	BO CTGTGGAC	1690 ATAAGC
	GCCAGGAGTCC 2380	CŤTĊAĊĊĂTĂĀ 2390	TGČČCÁČČTĆ 2400	TCCTGTGATC 2410	CATAACTCA 2420	TGGGTGCCG1 2430	TGATTGGCAT 2440

FIG.35D

inputs	1700 TGGTGGGC TGCAGTGC	AGAA TGGGGACCCT	1710 TGTTGTTGTA TGTGGTGGCC	1720 CAAGTG CTGGTAGCAC	TGATTTTAG TGATTTATTG	.730 1 ATCGATTT CTACCGACAC	740 TTTTTTAAAGT- TGGCAAAAGGGC
	2450 750 ATGTGTTG	2460 1760 GGTAC-CTTT	2470 1770 TCTGTG-TGT	2480 1780 ATGCTCAGG	2490 1790 CAGGCTGTGTG	2500 1800 STGTCTCTAGT	2510 1810 TGGCTTTAGAG
	AAGGAACA 2520	TGAGCACTTG 2530	GCAGTGGCTA 2540	CAGCACTGGG 2550	CGACTGGATG 2560	GCŤČ-ČGÁTŤ 2570	ACĠTCATĠCCA 2580
•	GATGTCTC 2590	TCCGĂĠCŤÁC 2600	ÄĞTCÄCTÄCT 2610	ATTCĊAACCC 2620	TAGCTÁCCÁC 2630	AČÁCŤĠŤĊŤC 2640	
inputs	-CCAAGCT ACCCTCCA 2660	BO 18 TAACTAGTTA CCCCCTAACA 2670	90 GAGCTCCA ÀĠÁTTCCÁGG 2680	1900 CCAGCAG CAGTCAGCTG 2690	1 iCAG-G iTTTGTCAGCT 2700	910 CCCTAACTAC CCCAGGCATC 2710	1920 CTGCCTGC TGAGCGGCCAAA 2720
	ČAGAAAČĆ 2730	ATGGGĊGÄĠĀ 2740	TÄÄCCÄČGČC 2750	ÁCÁĊŤGCCĊG 2760	ĊŢĠĀĊŢĠĠĀĀ 2770	ĠĊĂĊĊĠĂĊĠĠŒ 2780	GAGTCCCATGAC 2790
4.	2800	2810	2820	2830	2840	2850	AGGAATGGCCG 2860
inputs	2030 TCTTG	2040 CT-TCATT	CTTTCC	2050 CAGAATGAAG	2060 GCTGTCTGCC	2070 ACCCTACT-TO	2080 CCAGCCCAGGA
	GGGCCATT 2870	CTGTCATAAA 2880	GGTCCCÁTCT 2890	CTGAAGAAGG 2900	ÁĊTÁGGGĠĊA 2910	AGCGTTATGTO 2920	CCCTGAGCAGTG 2930
inputs	A20	90 2 TTGGCACA	100 TCTAAGTTCA	2110 GCCTT	2120 CCTAAGTTAC	2130 CCGTTGAGTC	2140 CTGCTTGCCCTT
	AGAACCCC 2940	TÁTĠĊĠĄCĊĀ 2950	ŤĊĊĠĂĠĂĊĊŤ 2960	GCCCGGCCTG 2970	CCTGGGGAAC 2980	CCCGAGAAAG 2990	ÄĞCTÄTGTGGÄ 3000
inputs	2150 CACATAT-	TCCA-C	2160 AGAA-CACCC	ACC0	.70 21 CACATCTGCT	80 219 TCATAGCTAC	2200 CCTCTTCTCCAC CAGCAGCAG
	GATGAAAG 3010	GCCCTCCATC 3020	3030	3040	3050	CCGGGACAGG 3060	CAGCÁGCÁA 3070
٠.			F	IG.35	E		

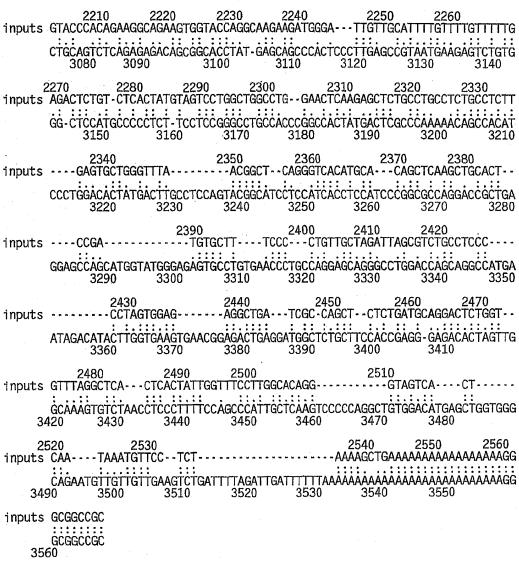


FIG.35F

		10 2	0	30	40	50	60 70
inputs	MAPARAGEC	PLLLLLLGL	WVAEIPVSA	KPKGMTSS	QWFKIQHMQPS	SPQACNSAMKN:	INKHTKRCKDLNT
		FPLLLLLLVL	WGPVCPLHA	WPKRLTKA	HWFEIQHIQP:	SPLQCNRAMSG:	INNYAQHCKHQNT
		10	20	30	40	50	60
	_	9	-	.00	110		130 140
inputs							KSYVVACKPPQKK
							:::: :::: KFFIVACDPPQKS
	70	80	90	100	110	120	130
*	15	50					
inputs	DSQQFHLVF	VHLDRVL					
	DPP-YKLMVI						
	140	150					

FIG.36

inputs	GTCGACC		20 GGCTCCCAGC	30 CCACCCCCAA	40 ACAGACACAG		60 GCCAGCTCTTAAGG ĠĠ
inputs	AGTTCAG ŤĠ	80 GAGTGAGAA	90 GAGGCCCTCA(	100 GAGATCTGAC	110 AĞCCTAGGAG ĊTA	120 TGCGTGGACAC TĠĊTTTĊ	130 CACCTCAGCCCAC CCTCTCT
inputs	TGAGCAG	150 GAGTCACAG	160 CACGAAGACCA	170 AAGCGCAAAG	180 CĠACCCCTGC ĊŤĠĊ	190 CCTCCATCCTC	200 ACTGCTCCTCCTA TĠĠTŤĊŤÅ 40
inputs	AGAGAGA TĠĠĠ	220 TGGCACCGG ĠÅ	230 CCAGAGCAGG/ CCAĠŤĠ 50	240 ATTCTGCCCC †ĠTĊĊAI	250 CTTCTGCTGC ĊŤŤĊÅŤĠĊ	260 TTCTGCTGCTG †† 70	270 <u>280</u> GGGGCTGTGGGTGG ĠĠĊ
inputs	CAGAGAT ĊŤÅÅĠ	290 CCCAGTCAG Ċ-ĠŤĊŤ- 80	300 TGCCAAGCCC/ ĊÀĊĊ/	310 AAĞĞĞCATĞA ĀĞĞ-Ö 90	320 CCTCATCACA †ĊÁĊ-	330 GTGGTTTAAA/ - TĠĠŤŤŤĠÁÁ/ 100	340 ATTCAGCACATĞCA ATTCAĞCATATACA 110
inputs	GCCCAGO ĠĊĊAĀĠT 120	360 CCTCAAGCA CCTCT 130	370 TGCAACTCAG(	380 CCATGAAAAA CCA	390 CATTAACAAG ÀTĠ	400 CACACAAAAC CAÀCA 140	410 GGTGCAAAGACCTC AGGGCÄÄTGÄ 150
inputs							480 AATAGCCTGCAAGA ITATGCC 170
inputs							550 CTCACCTCAGGGAA ĊĀĊĠĀ
inputs	GTATCCG ÁÁTÁCCT 90	570 AACTGCAGG TTCTGCÁTG 200	580 TACAAAGAGA -ÀĊ	590 AGCGACAGAA	600 CAAGTCTTAC †ċ†††ċ 210	610 GTAGTGGCCTC	620 GTAAGCCTCCCAG ĊĀĠ
	AAAAAGG	640 SACTCTCAGC	650 AATTCCACCT	660 GGTTCCTGTA	670 CACTTGGACA	680 GAGTCCTTTA(	690 GGTTTCCAGACTGG ĠAŤŤŤĠĊŤĊĀĠ- 240

# FIG.37A

inputs	CTTGCTCTT	io TGGCTGACÓ TGTCTGC	/20 CTTCAATTC CAA-ÁÁÁŤĊ	730 CCTCTCCAGG	740 ACTCCGCACC ŤĊGĠĠĠĊ	750 ACTCCCCTAC ÁCTGCCA	760 CACCCAGAGO - CCAGAGO	770 ATTCT
inputs	CTTCCCCTC	0 ATCTCTTGG	790 GGCTGTTC	800 CTGGTTCAGC	810 CTCTGCTGG	820 AGGCTGAAGC -GÁCTGC 310	830 TGACACTCT	840 GGTGA
inputs	GCTGAGCTC	0 TAGAGGGAT	360 GGCTTTTC/	870 ATCTTTTTGT	880 TGCTGTTTTC	890 CCAGATGCTT	900 ATCCCCAAG	910 SAAACA
inputs	92 GCAAGCTCA	GGTCTGTGG	30 GTTCCCTG(	940 STCTATGCCA	950 TTGCACATGT	960 CTCCCCTGCC	970 CCCCTGGCAT	980 TAGGG
inputs	CAGCATGAC	0 AAGGAGAG	000 GAAATAAAT	LO10 GAAAGGGGG	1020 CATATGGGAT	1030 TTGTGGACAC	1040 AGCTGTTTC	1050 TGTTC
inputs	106 CTGAACTAG CAGTACAAA	0 10 AAGTCTTCC ††c††c-	70 CCAGCTCT	LO80 GACGTGGCAG	1090 TGAGGTGACO	1100 TGAAGGAAAG	1110 AAAAATATA	1120
inputs 38	ATACCACTT	0 11 CATATTTGT	40 ATAGAATC	L150 TCTAATCCC	1160 TTGTGACATA	1170 GACTTGACAG ĊŤĊÁĠ	1180 GGATTGTAT	1190 GCCTT
inputs		0 12 TG <u>AGGA</u> AAT	10 TAAGGTTT	L220 FAGAAAGCTT	1230 AATGAATTAA	1240 AGAGCTTGTC ĀĠĀĠĊ	1250 TAATTAGTT	1260 AGTAG
inputs	127 CAGAACCTG	0 12 GACTTGAAC	80 CTAGGTCT	L290 CTTGCTCTA	1300 AATACAGTGT	1310 ACCTTCTACT -ĊĊ	1320 CTACCAGTT	1330 GCGCA
inputs	134 AGAAAGAAG	.0 13 TCACTGTTA	50 CAGAGGCA	1360 AGCGGTGAAC	1370 TAGGTAAGAG	1380 TTCACTCATG TTCTCT 450	1390 AAGAAACGA	

# FIG.37B

nputs CTGAAGÄĞÜÜAGTTACÜÜTĞTGTTGGÜTĞÜAATAAAĞĞTÖATTACCTÜÜTÖTAGCCAÄÄÄAAAAAAAÄÄÄA
nputs AAAAAAÄÄÄAAAAAAAAAAAAAA

FIG.37C

43.4% identity in 477 aa overlap; score: 746

410 GGTGCAAAG---ACCTCAACACCTTC--CTGCACGAGCCTTTC--TCCAGTGTGGCCGCCACCTGCCAGA ĠĠŤĠĊŤĂŤĠCTTŤĊĊŤĊŤŤŤŤÁČŢĠĊŤĠĊŤĠĠŤŢĊŤÁŤGGGGAĊĊĂĠŤĠŤĠŤĊĊĂĊTŤĊAŤĠĊŢŤĠĠ 10

FIG.38A

46.5% identity in 488 aa overlap; score: 709

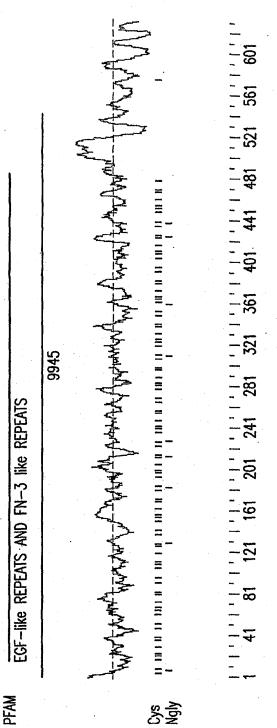
FIG.38B

ÁÁÁTÁCCTTTCTGCÁTGACT--CT--TTCCÁGÁÁ---TGTGGCTGCTGTGTGATTTGCTCÁGCATTGT

laminin EGF: domain 1 of 4, from 3 to 37: score -1.2, E = 0.59\*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrCdr.CkpG ++GqC+ C+ + +G+rC +C +G mT272 ---HASG----DP----- VHGQCR - CQAGWMGTRCHLpCPEG 31 yyg1psgdpgqgC<-\* <del>++</del>g + +0 mT272 32 FWG-----A-NC 37 EGF: domain 1 of 4, from 37 to 67: score 19.2, E = 0.1\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyylsytGkrC<-C+ ++ C+ngGtCv+ q C+C+pG CSNTCTCKNGGTCVSENG-----NCVCAPG----FRGPSC mT272 37 67 DSL: domain 1 of 1, from 10 to 67: score -21.2, E = 8.1\*->Wstdkhiggrts1Gfn1eyrirvtCdenYYGsgCnkFCrPrdDafgH +r+ Ce G+C++C ++ mT272 -- HGQCRCQAG----WMGTRCHLPCPEGFWGANCSNTCTCK---NGG 47 10 ytCdenGnk1CleGWkGeyC<-\* +enGn C++G +G+ C 48 TCVSENGNCVCAPGFRGPSC mT272 laminin EGF: domain 2 of 4, from 41 to 80: score -1.5, E = 0.63\*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrCdr.CkpG e G C+ C p++ G+ C r+C pG C+C + G tC s mT272 CTCKNGG-----TCVS-----ENGNCV-CAPGFRGPSCQRpCPPG 74 41 yyg1psgdpgqgC<-\* + + C 75 RY----GKR--C mT272 EGF: domain 2 of 4, from 80 to 110: score 11.8, E = 1.9\*->CapnnpCsng.GtCvntpggssdnfggytCeCppGdyylsytGkrC< C+n++ C+++ g Tc C G CVQC-KCNNNhSSCHPSDG-MT272 .80 -TCSCLAG----WTGPDC 110

laminin\_EGF: domain 3 of 4, from 83 to 123: score 25.6, E = 0.0012\*->CdCnphGalsddtCdsddelfgeetGqClkCkpnvtGrrC.drCkpG C Cn++ <del>++</del>C++ +G C+ C+ + tG++C++ C pG mT272 83 CKCNNNH----SSCHP-----SDGTCS-CLAGWTGPDCsEACPPG 117 yyg1psgdpgqgC<-\* ++g1 C mT272 HWGL-----KC 123 118 EGF: domain 3 of 4, from 123 to 153: score 27.3, E = 0.00036\*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyylsytGkrC<-C++++ C++gGtc++ g +C+C+pG CSQLCQCHHGGTCHPQDG-----SCICTPG----WTGPNC mT272 123 153 laminin EGF: domain 4 of 4, from 127 to 172: score -5.5, E = 1.4\*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrC.drCkpG GCCp+tG++C+CpC+C++ G tC++ mT272 127 CQCHHGG-----TCHP------QDGSCI-CTPGWTGPNC1EGCPPR 160 yyglpsg.dpgqgC<-\* +g +1++ ++C 161 MFG-VNCsQLC-QC mT272 172 EGF: domain 4 of 4, from 166 to 196: score 4.5. E = 5.8 \*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<-C++++ C+ g C++ g +G +C C+CppG CSQLCQCDLGEMCHPETG------ACVCPPG-----HSGADC mT272 166 196

FIG.39B



*->CaPnnpC C++++ C ratT272 18 !ECRC	snqGtCvntpggssdntggytCeCppGayylsytGkrC<- +ngG C g +C+C+pG y+G+rC HNGGLCDRFTGQCHCAPGYIGDPRC	48
laminin_EGF: domain 1 of 11,	from 22 to 61: score 12.3, E = 0.038	
*->CdCnphG C C++ G ratT272 22 CRCHNGG	slsddtCdsddelfgeetGqClkCkpnvtGrrC.drCkpG Cd+ +tGqC+ C p++ G+rC+++C G LCDRFTGQCH-CAPGYIGDRCrEECPVG	<b>5</b> 5
yyg1psgdpg +g ratT272 56 RFG	a+C	
EGF: domain 2 of 11, from 61	to 91: score 18.3, E = 0.18	
*->CapnnpC Ca+++ C ratT272 61 CAETCDC	sngGtCvntpggssdnfggytCeCppGdyylsytGkrC<- q++C + q C C +G +tG+rC APGARCFPANGACLCEHGFTGDRC	91
<pre>laminin_EGF: domain 2 of 11,</pre>	from 65 to 105: score 4.0, E = 0.2	
CdC p +	slsddtCdsddelfgeetGqClkCkpnvtGrrCdrCkp +C + G+Cl C +++tG+rC ++ C + RCFPANGACL-CEHGFTGDRCTErlCPD	98
Gyyglpsgdp G ygl ratT272 99 GRYGL	+C	
EGF: domain 3 of 11, from 105	to 137: score 4.1, E = 9.6	
C++++ C	sngGtCvntpggssdnfggytCeCppGdyylsytGkrC + ++ C++ +g +C C+pG ++G +C DPEhsLSCHPMHGECSCQPGWAGLHC	137
laminin_EGF: domain 3 of 11,	from 109 to 150: score 13.1, E = 0.032	
C+C+p	slsddtCdsddelfgeetGqClkCkpnvtGrrCdr.CkpG sls C++ ++G+C+ C+p ++G +C+++C SLSCHPMHGECS-CQPGWAGLHCNEsCP	142
yyglpsgdpq ++ + g ratT272 143QDTHG	gC AGC 150	
	FIG.41A	

30, 33	
EGF: domain 4 of 11, from 150 to 180: score 27.7, $E = 0.00026$	
*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyylsytGkrC<- C++++ C++gG+C+ g C+C+pG ytG++C ratT272 150 CQEHCLCLHGGVCLADSGLCRCAPGYTGPHC	180
laminin_EGF: domain 4 of 11, from 154 to 193: score 8.4, E = 0084	
*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrC.drCkpG C C +hg + C +G C+ C p++tG++C + C p+ ratT272 154 CLC-LHGGVCLADSGLCR-CAPGYTGPHaNLCPPN	187
yyg1psgdpgqgC<-* *yg +C ratT272 188 TYGINC 193	
EGF: domain 5 of 11, from 193 to 223: score 10.6, E = 2.5	
*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<- C++++ C n C ++ g tC+C++G ++ +C ratT272 193 CSSHCSCENAIACSPVDGTCICKEGWQRGNC	223
laminin_EGF: domain 5 of 11, from 197 to 236: score 0.7, E = 0.4	
*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrCdr.CkpG C C ++ C ++ G C Ck++ + +C +C pG ratT272 197 CSCENAIACSPVDGTCI-CKEGWQRGNCSVpCPPG	230
yyglpsgdpgqgC<-* ++g+ +C ratT272 231 TWGSC 236	
EGF: domain 6 of 11, from 236 to 266: score 11.8, E = 1.9	
*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<- C+ + C + G+C + g C+C+pG + G +C ratT272 236 CNASCQCAHEGVCSPQTGACTCTPGWRGVHC	266
laminin_EGF: domain 6 of 11, from 240 to 279: score -2.2, E = 0.73	
*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrCdr.CkpG C+C + G C + tG+C C p+ G +C +C G ratT272 240 CQCAHEGVCSPQTGACT-CTPGWRGVHCQLpCPKG	273
yyglpsgdpgqgC<-* +g +gC ratT272 274 QFGEGC 279	

# FIG.41B

DSL:	domain 1	of 1,	, from 2	46 to 30	9: score	-19.4, E	= 5.2		
	ratT272	246	+ +	+++a+ t	+++	C + ·	YGegCnkFCrl +GegC+ C+ FGEGCASVCD	¯H.	287
	ratT272	288	yt.Cd.e + +Cd+ SDgCDpV	+G +C +	eGWkGeyC<- +GW+G C AGWMGTRC	* 309			
EGF:	domain 7	of 13	l, from	279 to 3	309: score	7.0, E	= 5.3		
	ratT272	279	Ca+ ∙	+ C++	C +++g	+C·	eCppGdyyls; +C+ G RCQAG\	+ G rC	309
lamir	nin_EGF:	domair	n 7 of 1	1, from	283 to 32	2: score	12.7, E =	0.035	
	ratT272	283	*->CdCn CdC+ CDCD	phGs1sdo h+ o -HS[	dtCdsddelf 1 Cd+ DGCDP	geetGqC7 ++G+C+ VHGHCR	kCkpnvtGrr( C+ + +G+r( -CQAGQMGTR(	Cdr.CkpG C +C +G CHLpCPEG	316
	ratT272	317	yyglpsg ++g FWG	+ +C	.*				
EGF:	domain 8	of 11	l, from	3 <b>22</b> to 3	352: score	17.3, E	= 0.38		
	ratT272	322	C+. ·	+ C+ngGt	:Cv+ g	· C-	eCppGdyylsy +C+pG VCAPG	+ G+ C	352
lamir	nin_EGF:	domair	1 8 of 1	1, from	326 to 36	5: score	-1.8, E =	0.67	
	ratT272	326	C+C	+ G	tC +	¯ e G C+	kCkpnvtGrr( C p++ G+ ( -CAPGFRGPS(	Cr+CpG	359
	ratT272	360	yyglpsg y RY	+ + C	365				
EGF:	domain 9	of 11	L, from	365 to 3	394: score	18.3, E	= 0.18		
	ratT272	365	Ср	C+n+	C+++ q	tC	eCppGdyyls; C G SCLAGV	+tG++C	394

# FIG.41C

Taminin_EGF: domain 9 of 11, from 368 to 407: score 24.0, E = 0.0034	
*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrC.drCkpG C Cn+h+ +C++ + G C+ + + tG++C++ C pG ratT272 368 CKCNNHSSCHPSDGTCS-CLAGWTGPDCsESCPPG 40	-01
yyg]psgdpgqgC<-* ++g] C ratT272 402 HWGLKC 407	
EGF: domain 10 of 11, from 407 to 437: score 24.0, E = 0.035	
*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<- C++++ C++g+tC++ g +C+C pG +tG++C ratT272 407 CSQPCQCHHGATCHPQDGSCVCIPGWTGPNC 43	37
Taminin 505, demain 10 of 14 form 407 to 407, some 6.5.5 m. 0.10	
Taminin_EGF: domain 10 of 11, from 407 to 437: score 6.5, $E = 0.12$	
*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrCdrCkpGy C+C++ + tC++ G C+ C p+ tG++C + ratT272 411 CQCHHGATCHPQDGSCV-CIPGWTGPNCSE 43	39
yglpsgdpgggC<-* g ps+++g++C ratT272 440 -GCPSRMFGVNC 450	
EGF: domain 11 of 11, from 450 to 480: score 8.7, E = 3.7	
*->CapnnpCsngGtCvntpggssdnfggytCeCppGdyy1sytGkrC<- C++++ C+ g C++ g C+CppG +G +C ratT272 450 CSQLCQCDPGEMCHPETGACVCPPGHSGAHC 48	80
Taminin_EGF: domain 11 of 11, from 454 to 489: score -6.3, $E = 1.7$	
*->CdCnphGslsddtCdsddelfgeetGqClkCkpnvtGrrCdrCkpGy C+C+p G + C++ etG+C+ C p+ +G +C ratT272 454 CQCDP-GEMCHPETGACV-CPPGHSGAHCK 48	81
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# FIG.41D

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                                                                      180
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														cct Pro 185		1779	
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						_								att Ile		1875	
														att Ile		1923	
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130

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Jaar		a	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	-aay:	<b>50 0</b> 0		ישממי		2020		auut	22	-aa ;	20025	juayee	2022

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Ala Pro Cys Asp Pro Gln Thr Gly Ala Cys Phe Cys Pro Ala Glu Arg

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DIAGRAPHA, KANL VIENO (1941 185)

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60

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<213> Rauttus sp.

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ttg Leu	ccg Pro	Lys	gag Glu 260	gac Asp	att Ile	tcc Ser	tat Tyr	gca Ala 265	tct Ser	ctg Leu	acc Thr	ttg Leu	ggt Gly 270	gct Ala	gag Glu		877
gat Asp	cag Gln	gaa Glu 275	ccg Pro	acc Thr	tac Tyr	tgc Cys	aac Asn 280	atg Met	Gly	cac His	ctc Leu	agt Ser 285	agc Ser	cac	ctc Leu		925
														agc Ser			973
cct Pro 305	tago	ctgo	cac t	ccaç	gete	ec tt	cttg	gaco	c cca	ıggct	gtg	agca	acact	cc		:	1026
gggd gggd tato caca gtga gaga cata gggt aato	geete ettet eagge eatte etgt etage eaggat gatt eatte	yat o	cagoo gagtt atgot atcat ggct cotto ggtta aggco	cagos cotgo cotgo cotgo cotgo cotgo cotgo	tttggactaggaggaggaggagg	recece tette catt gge gaaa tgat caaa catga catga	tago laacg latos locos loggs ltcago latgo laaas ltggo	tot tot gas a tas a cas gts cas cas cas cas cas cas cas ca	egggt eccto atgat ataca gatat gageo gagac gageo gageo gageo gageo gageo gageo	tgg gaa atg ctg caa caa ttc aat	gctt tcct gate aacc tgtc gtat aata gtga ctgc	gggggaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa	gec a cag to the cag t	agto agaa agaa atto ctcag aaggo aagto aaggo	ggtgcc etcagg gaggg aatgt gaacttt gacctt ggacgt gaaagg acttga etggt		1086 1146 1206 1266 1326 1386 1446 1506 1566 1626 1686 1746

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<213> Homo sapiens

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 Thr
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 Tyr
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 Leu
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 Pro
 Trp
 Leu
 Ser
 Gly
 Tyr

 Ser
 Ile
 Ala
 Thr
 Gln
 Ile
 Thr
 Gly
 Pro
 Thr
 Val
 Asn
 Gly
 Leu
 Glu
 Glu
 Ile
 Intraction
 Asn
 Intraction
 Intraction

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Ser Ile Lys Asp Asn Gln Lys Asn Arg Thr Phe Thr Val Thr Met Glu
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Asp Leu Met Lys Thr Asp Ala Asp Thr Tyr Trp Cys Gly Ile Glu Lys
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Thr Gly Asn Asp Leu Gly Val Thr Val Gln Val Thr Ile Asp Pro Ala
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Ser Thr Pro Ala Pro Thr Thr Pro Thr Ser Thr Thr Phe Thr Ala Pro
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Leu Asp Asn Arg His Lys Leu Leu Lys Leu Ser Val Leu Leu Pro Leu
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Trp Arg Met Met Lys Tyr Gln Gln Lys Ala Ala Gly Met Ser Pro Glu
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-			_	_	_	_				_	-			aca Thr 20		104
														gtg Val		152
			Ser		_				_				_	ctg Leu		200
	_		_									_		ttg Leu	_	248
														ttc Phe		296
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	_		_			_		-	***					gag Glu	-	392
		_	_	_	_		_				_			atc Ile	_	440
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															cag Gln		872	
					_			_		_		-		~ ~	ctg Leu		920	
•															cct Pro		968	
	ccc Pro 310	gjà aaa	tca Ser	gca Ala	tgc Cys	acg Thr 315	gct Ala	ctg Leu	gcc Ala	gct Ala	gcc Ala 320	ctg Leu	cac His	tac Tyr	gcg Ala	ctg Leu 325	1016	
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															gtc Val		1208	
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			ttc Phe							_	tagt	ceg	ggc	ctcct	:ggcc1	b	1645
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                                         475
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                                     490
Phe Phe Leu Phe Leu Trp Phe Cys Ser Gln Arg Cys Arg Ser Glu Ala
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25

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<210> 40 <211> 79 <212> PRT <213> Homo sapiens

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Val Phe Ile Leu Gly Thr Leu Leu Leu Trp 1 5 10

<210> 44 <211> 116 <212> PRT <213> Homo sapiens

Tyr Val Glu Ile Arg Asp Gly Asp Pro Ser Ser Pro Leu Leu Gly Arg 65 - 70 - 75 - 80

Phe Cys Gly Ser Gly Lys Pro Glu Asp Ile Arg Ser Thr Ser Asn Arg 90 - 95

Met Leu Ile Lys Phe Val Ser Asp Ala Ser Val Ser Lys Arg Gly Phe 105 Ala Thr Tyr 115 - 115

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Pro Asn Val Thr Gly Arg Arg Cys Asp Arg Cys Lys Pro Gly Tyr Tyr
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Gly Leu Pro Ser Gly Asp Pro Gln Gln Gly Cys
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Gln Gly Ser Cys Ser Cys Pro Pro Gly Trp Met Gly Thr Ile Cys
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Ser Cys Leu Pro Gly Trp Ala Gly Leu His Cys
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Thr Gly Ala Cys Thr Cys Thr Pro Gly Trp His Gly Ala His Cys
                                25
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<210> 58 <211> 31 <212> PRT <213> Homo sapiens <400> 58 Cys Ala Ser Arg Cys Asp Cys Asp His Ser Asp Gly Cys Asp Pro Val 1. 5 10 His Gly Arg Cys Gln Cys Gln Ala Gly Trp Met Gly Ala Arg Cys 25 <210> 59 <211> 31 <212> PRT <213> Homo sapiens <400> 59 Cys Ser Asn Thr Cys Thr Cys Lys Asn Gly Gly Thr Cys Leu Pro Glu 10 Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys 25 <210> 60 <211> 30 <212> PRT <213> Homo sapiens <400> 60 Cys Val Pro Cys Lys Cys Ala Asn His Ser Phe Cys His Pro Ser Asn 10 Gly Thr Cys Tyr Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys 20 25 <210> 61 <211> 31 <212> PRT <213> Homo sapiens <400> 61 Cys Ala Gln Thr Cys Gln Cys His His Gly Gly Thr Cys His Pro Gln 10 Asp Gly Ser Cys Ile Cys Pro Leu Gly Trp Thr Gly His His Cys <210> 62 <211> 31 <212> PRT <213> Homo sapiens <400> 62 Cys Ser Gln Pro Cys Gln Cys Gly Pro Gly Glu Lys Cys His Pro Glu 5 10 Thr Gly Ala Cys Val Cys Pro Pro Gly His Ser Gly Ala Pro Cys 20 25

الكائل المخافية ومهادمها ومهل إربياف مجاره ومهابها فالمعد فاكوون

<210> 63 <211> 37 <212> PRT

### <213> Homo sapiens

<400> 63 Gln Thr Gly Ala Cys Thr Cys Thr Pro Gly Trp His Gly Ala His Cys 10 Gln Leu Pro Cys Pro Lys Gly Gln Phe Gly Glu Gly Cys Ala Ser Arg 20 25 Cys Asp Cys Asp His 35 <210> 64 <211> 31 <212> PRT <213> Mus musculus <400> 64 Cys Ser Asn Thr Cys Thr Cys Lys Asn Gly Gly Thr Cys Val Ser Glu 1 5 10 Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys 25 <210> 65 <211> 31 <212> PRT <213> Mus musculus <400> 65 Cys Val Gln Cys Lys Cys Asn Asn His Ser Ser Cys His Pro Ser 1 5 10 Asp Gly Thr Cys Ser Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys 25 <210> 66 <211> 31 <212> PRT <213> Mus musculus <400> 66 Cys Ser Gln Leu Cys Gln Cys His His Gly Gly Thr Cys His Pro Gln 5 10 Asp Gly Ser Cys Ile Cys Thr Pro Gly Trp Thr Gly Pro Asn Cys 20 <210> 67 <211> 31 <212> PRT <213> Mus musculus <400> 67 Cys Ser Gln Leu Cys Gln Cys Asp Leu Gly Glu Met Cys His Pro Glu 5 10 Thr Gly Ala Cys Val Cys Pro Pro Gly His Ser Gly Ala Asp Cys 20 25

<210> 68

<211> 35

<212> PRT

<213> Mus musculus

```
<400> 68
His Ala Ser Gly Asp Pro Val His Gly Gln Cys Arg Cys Gln Ala Gly
                5
                                   10
Trp Met Gly Thr Arg Cys His Leu Pro Cys Pro Glu Gly Phe Trp Gly
                               25
Ala Asn Cys
       35
      <210> 69
     <211> 40
      <212> PRT
      <213> Mus musculus
      <400> 69
Cys Thr Cys Lys Asn Gly Gly Thr Cys Val Ser Glu Asn Gly Asn Cys
                                10
Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys Gln Arg Pro Cys Pro
          20
Pro Gly Arg Tyr Gly Lys Arg Cys
       35
     <210> 70
      <211> 35
      <212> PRT
      <213> Mus musculus
     <400> 70
Cys Lys Cys Asn Asn Asn His Ser Ser Cys His Pro Ser Asp Gly Thr
        5
                                10
Cys Ser Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys Ser Glu Ala Cys
                               25
Pro Pro Gly
       35
      <210> 71
      <211> 34
      <212> PRT
     <213> Mus musculus
     <400> 71
Cys Gln Cys His His Gly Gly Thr Cys His Pro Gln Asp Gly Ser Cys
                5
                                   10
Ile Cys Thr Pro Gly Trp Thr Gly Pro Asn Cys Leu Glu Gly Cys Pro
Pro Arg
      <210> 72
      <211> 58
      <212> PRT
      <213> Mus musculus ·
      <400> 72
His Gly Gln Cys Arg Cys Gln Ala Gly Trp Met Gly Thr Arg Cys His
                                   10
1
Leu Pro Cys Pro Glu Gly Phe Trp Gly Ala Asn Cys Ser Asn Thr Cys
                               25
Thr Cys Lys Asn Gly Gly Thr Cys Val Ser Glu Asn Gly Asn Cys Val
```

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45
Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys
                      55
      <210> 73
      <211> 28
     <212> PRT
     <213> Rattus sp.
     <400> 73
Glu Cys Arg Cys His Asn Gly Gly Leu Cys Asp Arg Phe Thr Gly Gln
                                10
Cys His Cys Ala Pro Gly Tyr Ile Gly Asp Arg Cys
        20
      <210> 74
      <211> 31
     <212> PRT
      <213> Rattus sp.
     <400> 74
Cys Ala Glu Thr Cys Asp Cys Ala Pro Gly Ala Arg Cys Phe Pro Ala
                                10
Asn Gly Ala Cys Leu Cys Glu His Gly Phe Thr Gly Asp Arg Cys
           20
                               25
     <210> 75
     <211> 33
     <212> PRT
    <213> Rattus sp.
     <400> 75
Cys Gln Asp Pro Cys Thr Cys Asp Pro Glu His Ser Leu Ser Cys His
                               10
Pro Met His Gly Glu Cys Ser Cys Gln Pro Gly Trp Ala Gly Leu His
           20
                               25
                                                   30
Cys
      <210> 76
      <211> 31
      <212> PRT
      <213> Rattus sp.
      <400> 76
Cys Gln Glu His Cys Leu Cys Leu His Gly Gly Val Cys Leu Ala Asp
               5
                                 10
Ser Gly Leu Cys Arg Cys Ala Pro Gly Tyr Thr Gly Pro His Cys
          20
                               25
      <210> 77
      <211> 31
      <212> PRT
      <213> Rattus sp.
      <400> 77
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10

Cys Ser Ser His Cys Ser Cys Glu Asn Ala Ile Ala Cys Ser Pro Val

```
Asp Gly Thr Cys Ile Cys Lys Glu Gly Trp Gln Arg Gly Asn Cys
      <210> 78
      <211> 31
      <212> PRT
      <213> Rattus sp.
     <400> 78
Cys Asn Ala Ser Cys Gln Cys Ala His Glu Gly Val Cys Ser Pro Gln
                                    10
Thr Gly Ala Cys Thr Cys Thr Pro Gly Trp Arg Gly Val His Cys
                                25
      <210> 79
      <211> 31
      <212> PRT
      <213> Rattus sp.
      <400> 79
Cys Ala Ser Val Cys Asp Cys Asp His Ser Asp Gly Cys Asp Pro Val
                                    10
His Gly His Cys Arg Cys Gln Ala Gly Trp Met Gly Thr Arg Cys
      <210> 80
      <211> 31
      <212> PRT
      <213> Rattus sp.
      <400> 80
Cys Ser Asn Ala Cys Thr Cys Lys Asn Gly Gly Thr Cys Val Pro Glu
                                    10
Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys
            20
                                25
      <210> 81
      <211> 30
      <212> PRT
      <213> Rattus sp.
      <400> 81
Cys Val Pro Cys Lys Cys Asn Asn His Ser Ser Cys His Pro Ser Asp
                                    10
Gly Thr Cys Ser Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys
            20
                                25
      <210> 82
      <211> 31
      <212> PRT
      <213> Rattus sp.
      <400> 82
Cys Ser Gln Pro Cys Gln Cys His His Gly Ala Thr Cys His Pro Gln
                 5
                                    10
Asp Gly Ser Cys Val Cys Ile Pro Gly Trp Thr Gly Pro Asn Cys
```

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<210> 83 <211> 31 <212> PRT <213> Rattus sp. <400> 83 Cys Ser Gln Leu Cys Gln Cys Asp Pro Gly Glu Met Cys His Pro Glu 10 Thr Gly Ala Cys Val Cys Pro Pro Gly His Ser Gly Ala His Cys 25 <210> 84 <211> 40 <212> PRT <213> Rattus sp. <400> 84 Cys Arg Cys His Asn Gly Gly Leu Cys Asp Arg Phe Thr Gly Gln Cys 5 10 His Cys Ala Pro Gly Tyr Ile Gly Asp Arg Cys Arg Glu Glu Cys Pro 20 25 Val Gly Arg Phe Gly Gln Asp Cys 35 <210> 85 <211> 39 <212> PRT <213> Rattus sp. <400> 85 Cys Asp Cys Ala Pro Gly Ala Arg Cys Phe Pro Ala Asn Gly Ala Cys 5 10 Leu Cys Glu His Gly Phe Thr Gly Asp Arg Cys Thr Glu Arg Leu Cys 20 25 Pro Asp Gly Tyr Gly Leu Cys 35 <210> 86 <211> 42 <212> PRT <213> Rattus sp. <400> 86 Cys Thr Cys Asp Pro Glu His Ser Leu Ser Cys His Pro Met His Gly 10 Glu Cys Ser Cys Gln Pro Gly Trp Ala Gly Leu His Cys Asn Glu Ser 20 25 Cys Pro Gln Asp Thr His Gly Ala Gly Cys 35 <210> 87 <211> 40 <212> PRT <213> Rattus sp.

10

Cys Leu Cys Leu His Gly Gly Val Cys Leu Ala Asp Ser Gly Leu Cys

<400> 87

Arg Cys Ala Pro Gly Tyr Thr Gly Pro His Cys Ala Asn Leu Cys Pro 20 Pro Asn Thr Tyr Gly Ile Asn Cys 35 <210> 88 <211> 40 <212> PRT <213> Rattus sp. <400> 88 Cys Ser Cys Glu Asn Ala Ile Ala Cys Ser Pro Val Asp Gly Thr Cys 10 Ile Cys Lys Glu Gly Trp Gln Arg Gly Asn Cys Ser Val Pro Cys Pro 20 Pro Gly Thr Trp Gly Phe Ser Cys 35 <210> 89 <211> 40 <212> PRT <213> Rattus sp. <400> 89 Cys Gln Cys Ala His Glu Gly Val Cys Ser Pro Gln Thr Gly Ala Cys 5 10 Thr Cys Thr Pro Gly Trp Arg Gly Val His Cys Gln Leu Pro Cys Pro 20 Lys Gly Gln Phe Gly Glu Gly Cys 35 <210> 90 <211> 40 <212> PRT <213> Rattus sp. <400> 90 Cys Asp Cys Asp His Ser Asp Gly Cys Asp Pro Val His Gly His Cys 5 10 Arg Cys Gln Ala Gly Trp Met Gly Thr Arg Cys His Leu Pro Cys Pro 20 25 Glu Gly Phe Trp Gly Ala Asn Cys 35 <210> 91 <211> 40 <212> PRT <213> Rattus sp. <400> 91 Cys Thr Cys Lys Asn Gly Gly Thr Cys Val Pro Glu Asn Gly Asn Cys 10 Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys Gln Arg Pro Cys Pro 20 Pro Gly Arg Tyr Gly Lys Arg Cys 35

<210> 92

<211> 40 <212> PRT <213> Rattus sp. <400> 92 Cys Lys Cys Asn Asn His Ser Ser Cys His Pro Ser Asp Gly Thr Cys 10 Ser Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys Ser Glu Ser Cys Pro Pro Gly His Trp Gly Leu Lys Cys 35 <210> 93 <211> 40 <212> PRT <213> Rattus sp. <400> 93 Cys Gln Cys His His Gly Ala Thr Cys His Pro Gln Asp Gly Ser Cys 1. 5 10 Val Cys Ile Pro Gly Trp Thr Gly Pro Asn Cys Ser Glu Gly Cys Pro Ser Arg Met Phe Gly Val Asn Cys 35 <210> 94 <211> 36 <212> PRT <213> Rattus sp. <400> 94 Cys Gln Cys Asp Pro Gly Glu Met Cys His Pro Glu Thr Gly Ala Cys 5 10 Val Cys Pro Pro Gly His Ser Gly Ala His Cys Lys Val Gly Ser Gln 20 25 Glu Ser Phe Thr 35 <210> 95 <211> 64 <212> PRT <213> Rattus sp. <400> 95 Gly Val Cys Ser Pro Gln Thr Gly Ala Cys Thr Cys Thr Pro Gly Trp 1.0 Arg Gly Val His Cys Gln Leu Pro Cys Pro Lys Gly Gln Phe Gly Glu 20 25 Gly Cys Ala Ser Val Cys Asp Cys Asp His Ser Asp Gly Cys Asp Pro 40 45 Val His Gly His Cys Arg Cys Gln Ala Gly Trp Met Gly Thr Arg Cys 55 <210> 96 <211> 129

<212> PRT

<213> Homo sapiens

<400> 96 Gln Glu Ser Arg Ala Gln Lys Phe Leu Arg Gln His Ile Asp Ser Pro Lys Thr Ser Ser Ser Asn Pro Asn Tyr Cys Asn Gln Met Met Asp Lys 25 Arg Arg Asn Met Thr Gln Gln Arg Cys Lys Pro Val Asn Thr Phe Val 35 40 45 His Glu Ser Leu Ala Asp Val Lys Ala Val Cys Ser Gln Lys Asn Val 55 Thr Cys Lys Asn Gly Gln Ser Lys Ser Ser Phe Gln Ile Thr Asp Cys 70 Arg Leu Thr Gly Gly Ser Gln Lys Tyr Pro Asn Cys Arg Tyr Arg Thr Ser Ala Ser Thr Lys His Ile Ile Val Ala Cys Glu Gly Arg Asp Arg 105 Asp Asp Pro Tyr Tyr Asn Pro Tyr Val Pro Val His Phe Asp Ala Ser Val

<210> 97 <211> 125 <212> PRT <213> Homo sapiens

<400> 97 Gly Met Thr Ser Ser Gln Trp Phe Lys Ile Gln His Met Gln Pro Ser 5 10 Pro Gln Ala Cys Asn Ser Ala Met Lys Asn Ile Asn Lys His Thr Lys 20 Arg Cys Lys Asp Leu Asn Thr Phe Leu His Glu Pro Phe Ser Ser Val 40 Ala Ala Thr Cys Gln Thr Pro Lys Ile Ala Cys Lys Asn Gly Asp Lys 55 Asn Cys His Gln Ser His Gly Pro Val Ser Leu Thr Met Cys Lys Leu 70 75 Thr Ser Gly Lys Tyr Pro Asn Cys Arg Tyr Lys Glu Lys Arg Gln Asn 90 85 Lys Ser Tyr Val Val Ala Cys Lys Pro Pro Gln Lys Lys Asp Ser Gln 105 100 Gln Phe His Leu Val Pro Val His Leu Asp Arg Val Leu 115 120

<210> 98 <211> 411 <212> PRT <213> Homo sapiens

<213> Homo Bapiens

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Lys Lys Tyr Tyr Leu Val Leu Lys Ile Ile Tyr Thr Val Gly Tyr Ser
                                 90
              85
Leu Ser Leu Ala Ala Leu Leu Val Ala Val Val Ile Leu Leu Phe
                    105
         100
Arg Lys Leu His Thr Leu Trp Pro Asp Asn Ala Asp Gly Ala Leu Glu
                         120
     115
                                             125
Val Gly Ala Pro Trp Gly Ala Pro Phe Gln Val Arg Arg Ser Ile Arg
130 135 140
   130
                      135
                                          140
Cys Thr Arg Asn Tyr Ile His Met Asn Leu Phe Leu Ser Phe Ile Leu
                  150
                                      155
Arg Ala Ala Ser Val Phe Ile Lys Asp Ala Val Leu Lys Ser Glu Val
               165
                                  170
                                                      175
Ser Ser Asp Glu Pro Glu Arg Leu Ser Ser Arg Cys Ser Leu Ser Thr
          180
                             1.85
                                                 190
Gly Gln Val Val Gly Cys Lys Leu Leu Val Val Phe Gln Phe Gln
     1.95
                         200
                                              205
Tyr Cys Val Met Thr Asn Phe Phe Trp Leu Leu Val Glu Gly Leu Tyr
   210
                      215
                                         220
Leu His Thr Leu Leu Val Val Thr Phe Phe Ser Glu Arg Lys Tyr Leu
                   230
                                      235
Trp Trp Tyr Leu Leu Ile Gly Trp Gly Val Pro Leu Val Phe Val Thr
                                  250
               245
Val Trp Ala Ile Val Arg Leu Leu Phe Glu Asp Thr Gly Cys Trp Asp
                            265
         260
Ser Asn Gly Leu Ala Met Phe Pro Glu Ala Lys Met Cys Ile Trp Met
                        280
                                             285
     275
Ser Asp Asn Ser His Leu Trp Trp Ile Ile Lys Gly Pro Ile Leu Leu
                      295
                                         300
Ser Ile Leu Val Asn Phe Phe Leu Phe Ile Asn Ile Ile Arg Ile Leu
                  310
                                      315
Val Thr Lys Leu Arg Ala Ala Gln Thr Gly Glu Thr Asp Gln Arg Gln
               325
                                  330
Tyr Ser Gln Tyr Arg Lys Leu Ala Lys Ser Thr Leu Leu Leu Ile Pro
                              345
Leu Phe Gly Ile His Tyr Val Val Phe Ala Phe Arg Pro Ser Asn Asp
       355
                          360
                                              365
Ala Arg Gly Val Leu Arg Lys Ile Lys Leu Tyr Phe Glu Leu Ser Leu
                      375
                                         380
Gly Ser Phe Gln Gly Phe Phe Val Ala Val Leu Tyr Cys Phe Leu Asn
                  390
                                      395
Gly Glu Val Gln Ala Glu Ile Arg Arg Arg Trp
               405
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<210> 99 <211> 328 <212> PRT

<213> Homo sapiens

Ile Ser Leu Val Gly Cys Ser Ile Ser Ile Val Ala Ser Leu Ile Thr 70 Val Leu Leu His Phe Arg Lys Gln Ser Asp Ser Leu Thr Arg Ile His 85 90 Met Asn Leu His Ala Ser Val Leu Leu Leu Asn Ile Ala Phe Leu Leu 100 105 Ser Pro Ala Phe Ala Met Ser Pro Val Pro Gly Ser Ala Cys Thr Ala 115 120 Leu Ala Ala Leu His Tyr Ala Leu Leu Ser Cys Leu Thr Trp Met 135 140 Ala Ile Glu Gly Phe Asn Leu Tyr Leu Leu Leu Gly Arg Val Tyr Asn 150 155 Ile Tyr Ile Arg Arg Tyr Val Phe Lys Leu Gly Val Leu Gly Trp Gly 165 170 Ala Pro Ala Leu Leu Val Leu Leu Ser Leu Ser Val Lys Ser Ser Val 180 185 Tyr Gly Pro Cys Thr Ile Pro Val Phe Asp Ser Trp Glu Asn Gly Thr 195 200 205 Gly Phe Gln Asn Met Ser Ile Cys Trp Val Arg Ser Pro Val Val His 215 Ser Val Leu Val Met Gly Tyr Gly Gly Leu Thr Ser Leu Phe Asn Leu 225 230 235 Val Val Leu Ala Trp Ala Leu Trp Thr Leu Arg Arg Leu Arg Glu Arg 245 250 Ala Asp Ala Pro Ser Val Arg Ala Cys His Asp Thr Val Thr Val Leu 260 265 270 260 Gly Leu Thr Val Leu Leu Gly Thr Thr Trp Ala Leu Ala Phe Phe Ser 280 285 Phe Gly Val Phe Leu Leu Pro Gln Leu Phe Leu Phe Thr Ile Leu Asn 295 300 Ser Leu Tyr Gly Phe Phe Leu Phe Leu Trp Phe Cys Ser Gln Arg Cys 310 315 Arg Ser Glu Ala Glu Ala Lys Ala

<210> 100

<211> 150

<212> PRT

<213> Pan troglodytes

<400> 100

Met Val Leu Cys Phe Pro Leu Leu Leu Leu Leu Val Leu Trp Gly 10 Pro Val Cys Pro Leu His Ala Trp Pro Lys Arg Leu Thr Lys Ala His 20 25 Trp Phe Glu Ile Gln His Ile Gln Pro Ser Pro Leu Gln Cys Asn Arg 35 40 Ala Met Ser Gly Ile Asn Asn Tyr Ala Gln His Cys Lys His Gln Asn 55 60 Thr Phe Leu His Asp Ser Phe Gln Asn Val Ala Ala Val Cys Asp Leu 70 75 Leu Ser Ile Val Cys Lys Asn Arg Arg His Asn Cys His Gln Ser Ser 85 90 Lys Pro Val Asn Met Thr Asp Cys Arg Leu Thr Ser Gly Lys Tyr Pro 100 105 110 Gln Cys Arg Tyr Ser Ala Ala Ala Gln Tyr Lys Phe Phe Ile Val Ala 120 125 Cys Asp Pro Pro Gln Lys Ser Asp Pro Pro Tyr Lys Leu Val Pro Val

```
135
   130
                                           140
His Leu Asp Ser Ile Leu
     <210> 101
      <211> 24
      <212> PRT
      <213> Homo sapiens
      <400> 101
Met Thr Pro Ser Pro Leu Leu Leu Leu Leu Pro Pro Leu Leu Leu
1
               5
                                   10
Gly Ala Phe Pro Pro Ala Ala Ala
          20
     <210> 102
     <211> 480
      <212> PRT
     <213> Homo sapiens
     <400> 102
Ala Arg Gly Pro Pro Lys Met Ala Asp Lys Val Val Pro Arg Gln Val
Ala Arg Leu Gly Arg Thr Val Arg Leu Gln Cys Pro Val Glu Gly Asp
        20
                              25
Pro Pro Pro Leu Thr Met Trp Thr Lys Asp Gly Arg Thr Ile His Ser
 3.5
                          40
Gly Trp Ser Arg Phe Arg Val Leu Pro Gln Gly Leu Lys Val Lys Gln
                       55
Val Glu Arg Glu Asp Ala Gly Val Tyr Val Cys Lys Ala Thr Asn Gly
                   70
                                       75
Phe Gly Ser Leu Ser Val Asn Tyr Thr Leu Val Val Leu Asp Asp Ile
               85
                                  90
```

Ser Pro Gly Lys Glu Ser Leu Gly Pro Asp Ser Ser Ser Gly Gly Gln 100 105 110 Glu Asp Pro Ala Ser Gln Gln Trp Ala Arg Pro Arg Phe Thr Gln Pro 115 120 125 Ser Lys Met Arg Arg Arg Val Ile Ala Arg Pro Val Gly Ser Ser Val 135 140 Arg Leu Lys Cys Val Ala Ser Gly His Pro Arg Pro Asp Ile Thr Trp 150 155 Met Lys Asp Asp Gln Ala Leu Thr Arg Pro Glu Ala Ala Glu Pro Arg 165 170 Lys Lys Lys Trp Thr Leu Ser Leu Lys Asn Leu Arg Pro Glu Asp Ser 180 185 Gly Lys Tyr Thr Cys Arg Val Ser Asn Arg Ala Gly Ala Ile Asn Ala 200 Thr Tyr Lys Val Asp Val Ile Gln Arg Thr Arg Ser Lys Pro Val Leu 215 220 Thr Gly Thr His Pro Val Asn Thr Thr Val Asp Phe Gly Gly Thr Thr 230 235 Ser Phe Gln Cys Lys Val Arg Ser Asp Val Lys Pro Val Ile Gln Trp 250 245 Leu Lys Arg Val Glu Tyr Gly Ala Glu Gly Arg His Asn Ser Thr Ile 260 265 270 Asp Val Gly Gly Gln Lys Phe Val Val Leu Pro Thr Gly Asp Val Trp 275 280 Ser Arg Pro Asp Gly Ser Tyr Leu Asn Lys Leu Leu Ile Thr Arg Ala

```
295
Arg Gln Asp Asp Ala Gly Met Tyr Ile Cys Leu Gly Ala Asn Thr Met
                                  315
          310
Gly Tyr Ser Phe Arg Ser Ala Phe Leu Thr Val Leu Pro Asp Pro Lys
                       330
           325
Trp Pro Val Val Ile Gly Ile Pro Ala Gly Ala Val Phe Ile Leu Gly
      355
                     360
Thr Leu Leu Trp Leu Cys Gln Ala Gln Lys Lys Pro Cys Thr Pro
                    375
                                      380
Ala Pro Ala Pro Pro Leu Pro Gly His Arg Pro Pro Gly Thr Ala Arg
                 390
                                   395
Asp Arg Ser Gly Asp Lys Asp Leu Pro Ser Leu Ala Ala Leu Ser Ala
             405
                              410
Gly Pro Gly Val Gly Leu Cys Glu Glu His Gly Ser Pro Ala Ala Pro 420 425 430
Gln His Leu Leu Gly Pro Gly Pro Val Ala Gly Pro Lys Leu Tyr Pro 435
Lys Leu Tyr Thr Asp Ile His Thr His Thr His Thr His Ser His Thr
                  455
                                      460
His Ser His Val Glu Gly Lys Val His Gln His Ile His Tyr Gln Cys
                 470
                                   475
```

<210> 103 <211> 350 <212> PRT

<213> Homo sapiens

<400> 103 Ala Arg Gly Pro Pro Lys Met Ala Asp Lys Val Val Pro Arg Gln Val 10 Ala Arg Leu Gly Arg Thr Val Arg Leu Gln Cys Pro Val Glu Gly Asp Pro Pro Pro Leu Thr Met Trp Thr Lys Asp Gly Arg Thr Ile His Ser 35 40 Gly Trp Ser Arg Phe Arg Val Leu Pro Gln Gly Leu Lys Val Lys Gln 50 55 Val Glu Arg Glu Asp Ala Gly Val Tyr Val Cys Lys Ala Thr Asn Gly 75 70 Phe Gly Ser Leu Ser Val Asn Tyr Thr Leu Val Val Leu Asp Asp Ile 90 85 Ser Pro Gly Lys Glu Ser Leu Gly Pro Asp Ser Ser Ser Gly Gly Gln 100 105 110 100 105 110 Glu Asp Pro Ala Ser Gln Gln Trp Ala Arg Pro Arg Phe Thr Gln Pro 115 120 125 Ser Lys Met Arg Arg Arg Val Ile Ala Arg Pro Val Gly Ser Ser Val 135 140 Arg Leu Lys Cys Val Ala Ser Gly His Pro Arg Pro Asp Ile Thr Trp 150 155 Met Lys Asp Asp Gln Ala Leu Thr Arg Pro Glu Ala Ala Glu Pro Arg . 165 170 Lys Lys Lys Trp Thr Leu Ser Leu Lys Asn Leu Arg Pro Glu Asp Ser 180 185 Gly Lys Tyr Thr Cys Arg Val Ser Asn Arg Ala Gly Ala Ile Asn Ala 195 200 205 Thr Tyr Lys Val Asp Val Ile Gln Arg Thr Arg Ser Lys Pro Val Leu 215 220

```
Thr Gly Thr His Pro Val Asn Thr Thr Val Asp Phe Gly Gly Thr Thr
                   230
                                      235
Ser Phe Gln Cys Lys Val Arg Ser Asp Val Lys Pro Val Ile Gln Trp
                                  250
               245
Leu Lys Arg Val Glu Tyr Gly Ala Glu Gly Arg His Asn Ser Thr Ile
                              265
                                                 270
Asp Val Gly Gln Lys Phe Val Val Leu Pro Thr Gly Asp Val Trp
                                  285
      275
                      280
Ser Arg Pro Asp Gly Ser Tyr Leu Asn Lys Leu Leu Ile Thr Arg Ala
                    295
                                        300
Arg Gln Asp Asp Ala Gly Met Tyr Ile Cys Leu Gly Ala Asn Thr Met
                310
                                      315
Gly Tyr Ser Phe Arg Ser Ala Phe Leu Thr Val Leu Pro Asp Pro Lys
               325
                                 330
Pro Pro Gly Pro Pro Val Ala Ser Ser Ser Ser Ala Thr Ser
                              345
     <210> 104
     <211> 24
     <212> PRT
     <213> Homo sapiens
     <400> 104
Leu Pro Trp Pro Val Val Ile Gly Ile Pro Ala Gly Ala Val Phe Ile
1
            5
Leu Gly Thr Leu Leu Leu Trp Leu
         20
     <210> 105
     <211> 106
     <212> PRT
     <213> Homo sapiens
```

<400> 105

Cys Gln Ala Gln Lys Lys Pro Cys Thr Pro Ala Pro Ala Pro Pro Leu 5 10 Pro Gly His Arg Pro Pro Gly Thr Ala Arg Asp Arg Ser Gly Asp Lys 20 25 Asp Leu Pro Ser Leu Ala Ala Leu Ser Ala Gly Pro Gly Val Gly Leu 35 40 Cys Glu Glu His Gly Ser Pro Ala Ala Pro Gln His Leu Leu Gly Pro 55 60 Gly Pro Val Ala Gly Pro Lys Leu Tyr Pro Lys Leu Tyr Thr Asp Ile 70 75 His Thr His Thr His Thr His Ser His Thr His Ser His Val Glu Gly 85 Lys Val His Gln His Ile His Tyr Gln Cys

100 105

> <210> 106 <211> 208 <212> PRT

<213> Mus musculus

<400> 106 Arg Val Arg Pro Thr Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr 5 10 Leu Asn Lys Leu Leu Ile Ser Arg Ala Arg Gln Asp Asp Ala Gly Met

```
20
                               25
Tyr Ile Cys Leu Gly Ala Asn Thr Met Gly Tyr Ser Phe Arg Ser Ala
                           40
                                              45
Phe Leu Thr Val Leu Pro Asp Pro Lys Pro Pro Gly Pro Pro Met Ala
                      55
Ser Ser Ser Ser Thr Ser Leu Pro Trp Pro Val Val Ile Gly Ile
                   70
                                      75
Pro Ala Gly Ala Val Phe Ile Leu Gly Thr Val Leu Leu Trp Leu Cys
              85
                                  90
Gln Thr Lys Lys Lys Pro Cys Ala Pro Ala Ser Thr Leu Pro Val Pro
           100
                              105
Gly His Arg Pro Pro Gly Thr Ser Arg Glu Arg Ser Gly Asp Lys Asp
       115
                           120
                                              125
Leu Pro Ser Leu Ala Val Gly Ile Cys Glu Glu His Gly Ser Ala Met
                      135
                                         140
Ala Pro Gln His Ile Leu Ala Ser Gly Ser Thr Ala Gly Pro Lys Leu
                  150
                                      155
Tyr Pro Lys Leu Tyr Thr Asp Val His Thr His Thr His Thr His Thr
             165
                                170
Cys Thr His Thr Leu Ser Cys Trp Arg Ala Arg Phe Ile Asn Thr Ser
          1.80
                              185
                                                  190
Met Ser Thr Ile Ser Ala Lys Tyr Ser Glu Ser Pro Ser Thr Val Ser
       195
                           200
     <210> 107
     <211> 73
     <212> PRT
     <213> Mus musculus
     <400> 107
Arg Val Arg Pro Thr Gly Asp Val Trp Ser Arg Pro Asp Gly Ser Tyr
                                   10
Leu Asn Lys Leu Leu Ile Ser Arg Ala Arg Gln Asp Asp Ala Gly Met
                              25
                                                 30
Tyr Ile Cys Leu Gly Ala Asn Thr Met Gly Tyr Ser Phe Arg Ser Ala
       35
                          40
                                            45
Phe Leu Thr Val Leu Pro Asp Pro Lys Pro Pro Gly Pro Pro Met Ala
                55
                                          60
Ser Ser Ser Ser Thr Ser Leu Pro
                   70
     <210> 108
     <211> 23
     <212> PRT
     <213> Mus musculus
     <400> 108
Trp Pro Val Val Ile Gly Ile Pro Ala Gly Ala Val Phe Ile Leu Gly
               5
Thr Val Leu Leu Trp Leu Cys
           20
     <210> 109
     <211> 112
     <212> PRT
     <213> Mus musculus
     <400> 109
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```
Gln Thr Lys Lys Lys Pro Cys Ala Pro Ala Ser Thr Leu Pro Val Pro
                                    10
Gly His Arg Pro Pro Gly Thr Ser Arg Glu Arg Ser Gly Asp Lys Asp
           20
                                25
Leu Pro Ser Leu Ala Val Gly Ile Cys Glu Glu His Gly Ser Ala Met
     35
                           40
Ala Pro Gln His Ile Leu Ala Ser Gly Ser Thr Ala Gly Pro Lys Leu
  -50
                        55
                                           60
Tyr Pro Lys Leu Tyr Thr Asp Val His Thr His Thr His Thr His Thr
                  70
                                      75
Cys Thr His Thr Leu Ser Cys Trp Arg Ala Arg Phe Ile Asn Thr Ser
                                  90
               85
Met Ser Thr Ile Ser Ala Lys Tyr Ser Glu Ser Pro Ser Thr Val Ser
           100
                               105
     <210> 110
      <211> 35
      <212> PRT
     <213> Homo sapiens
     <400> 110
Met Pro Gly Pro Arg Val Trp Gly Lys Tyr Leu Trp Arg Ser Pro His
                                   10
Ser Lys Gly Cys Pro Gly Ala Met Trp Trp Leu Leu Leu Trp Gly Val
Leu Gln Ala
       35
     <210> 111
     <211> 103
     <212> PRT
     <213> Homo sapiens
     <400> 111
Cys Pro Thr Arg Gly Ser Val Leu Leu Ala Gln Glu Leu Pro Gln Gln
1
                                  1.0
Leu Thr Ser Pro Gly Tyr Pro Glu Pro Tyr Gly Lys Gly Gln Glu Ser
                               25
Ser Thr Asp Ile Lys Ala Pro Glu Gly Phe Ala Val Arg Leu Val Phe
       35
                           40
Gln Asp Phe Asp Leu Glu Pro Ser Gln Asp Cys Ala Gly Asp Ser Val
                       55
Thr Val Ser Trp Gly Trp Gly Gly Ser Arg Gln Asp Cys Gly Gln Gly
                                       75
Asp Ser Arg Gly Cys Gly Lys Trp Arg Cys Pro Glu Ser Pro Ile Trp
                                   90
               85
Arg Arg Asp Glu Phe Ser Met
           100
     <210> 112
     <211> 20
     <212> PRT
     <213> Homo sapiens
     <400> 112
```

10

Met Ser Pro Pro Leu Cys Pro Leu Leu Leu Ala Val Gly Leu Arg

3.

Leu Ala Gly Thr

<210> 113 <211> 1030 <212> PRT <213> Homo sapiens

<400> 113 Leu Asn Pro Ser Asp Pro Asn Thr Cys Ser Phe Trp Glu Ser Phe Thr 10 Thr Thr Lys Glu Ser His Ser Arg Pro Phe Ser Leu Leu Pro Ser 20 25 Glu Pro Cys Glu Arg Pro Trp Glu Gly Pro His Thr Cys Pro Ser Pro . 35 40 Gln Thr Gln Arg Lys Leu Leu Ala Ser Arg Asp Ser Phe Cys Met Val 55 Cys Val Gly Ala Gly Val Gln Trp Arg Asp Arg Ser Ala Leu Gln Pro 70 Gln Thr Gly Asn Ala Leu Ser Met Arg Pro Gln Pro Arg Val Leu Ser 90 Gly Ala Pro Ser Leu Ala Ser Pro Gly His Thr Val Val Val Lys Thr 100 105 710 Asp His Arg Gln Arg Leu Gln Cys Cys His Gly Phe Tyr Glu Ser Arg 1.20 125 115 Gly Phe Cys Val Pro Leu Cys Ala Gln Glu Cys Val His Gly Arg Cys 135 130 140 Val Ala Pro Asn Gln Cys Gln Cys Val Pro Gly Trp Arg Gly Asp Asp 145 150 150 155 150 155 Cys Ser Ser Ala Pro Asn Cys Leu Gln Pro Cys Thr Pro Gly Tyr Tyr 165 170 Gly Pro Ala Cys Gln Phe Arg Cys Gln Cys His Gly Ala Pro Cys Asp 180 185 190 Pro Gln Thr Gly Ala Cys Phe Cys Pro Ala Glu Arg Thr Gly Pro Ser 200 205 Cys Asp Val Ser Cys Ser Gln Gly Thr Ser Gly Phe Phe Cys Pro Ser 210 220 215 220 Thr His Pro Cys Gln Asn Gly Gly Val Phe Gln Thr Pro Gln Gly Ser 230 235 Cys Ser Cys Pro Pro Gly Trp Met Gly Thr Ile Cys Ser Leu Pro Cys 245 250 Pro Glu Gly Phe His Gly Pro Asn Cys Ser Gln Glu Cys Arg Cys His 260 265 270 Asn Gly Gly Leu Cys Asp Arg Phe Thr Gly Gln Cys Arg Cys Ala Pro 275 280 Gly Tyr Thr Gly Asp Arg Cys Arg Glu Glu Cys Pro Val Gly Arg Phe 290 295 300 Gly Gln Asp Cys Ala Glu Thr Cys Asp Cys Ala Pro Asp Ala Arg Cys 310 315 Phe Pro Ala Asn Gly Ala Cys Leu Cys Glu His Gly Phe Thr Gly Asp 325 330 335 Arg Cys Thr Asp Arg Leu Cys Pro Asp Gly Phe Tyr Gly Leu Ser Cys 340 345 350 Gln Ala Pro Cys Thr Cys Asp Arg Glu His Ser Leu Ser Cys His Pro 355 360 365 Met Asn Gly Glu Cys Ser Cys Leu Pro Gly Trp Ala Gly Leu His Cys 375 380 Asn Glu Ser Cys Pro Gln Asp Thr His Gly Pro Gly Cys Gln Glu His 390 . 395

Cys Leu Cys Leu His Gly Gly Val Cys Gln Ala Thr Ser Gly Leu Cys Gln Cys Ala Pro Gly Tyr Thr Gly Pro His Cys Ala Ser Leu Cys Pro Pro Asp Thr Tyr Gly Val Asn Cys Ser Ala Arg Cys Ser Cys Glu Asn Ala Ile Ala Cys Ser Pro Ile Asp Gly Glu Cys Val Cys Lys Glu Gly Trp Gln Arg Gly Asn Cys Ser Val Pro Cys Pro Pro Gly Thr Trp Gly Phe Ser Cys Asn Ala Ser Cys Gln Cys Ala His Glu Ala Val Cys Ser Pro Gln Thr Gly Ala Cys Thr Cys Thr Pro Gly Trp His Gly Ala His Cys Gln Leu Pro Cys Pro Lys Gly Gln Phe Gly Glu Gly Cys Ala Ser Arg Cys Asp Cys Asp His Ser Asp Gly Cys Asp Pro Val His Gly Arg Cys Gln Cys Gln Ala Gly Trp Met Gly Ala Arg Cys His Leu Ser Cys Pro Glu Gly Leu Trp Gly Val Asn Cys Ser Asn Thr Cys Thr Cys Lys Asn Gly Gly Thr Cys Leu Pro Glu Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys Gln Arg Ser Cys Gln Pro Gly Arg Tyr Gly Lys Arg Cys Val Pro Cys Lys Cys Ala Asn His Ser Phe Cys His 61.0 Pro Ser Asn Gly Thr Cys Tyr Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys Ser Gln Pro Cys Pro Pro Gly His Trp Gly Glu Asn Cys Ala Gln Thr Cys Gln Cys His His Gly Gly Thr Cys His Pro Gln Asp Gly Ser Cys Ile Cys Pro Leu Gly Trp Thr Gly His His Cys Leu Glu Gly Cys 67.5 Pro Leu Gly Thr Phe Gly Ala Asn Cys Ser Gln Pro Cys Gln Cys Gly Pro Gly Glu Lys Cys His Pro Glu Thr Gly Ala Cys Val Cys Pro Pro Gly His Ser Gly Ala Pro Cys Arg Ile Gly Ile Gln Glu Pro Phe Thr Val Met Pro Thr Thr Pro Val Ala Tyr Asn Ser Leu Gly Ala Val Ile Gly Ile Ala Val Leu Gly Ser Leu Val Val Ala Leu Val Ala Leu Phe Ile Gly Tyr Arg His Trp Gln Lys Gly Lys Glu His His Leu Ala Val Ala Tyr Ser Ser Gly Arg Leu Asp Gly Ser Glu Tyr Val Met Pro . 790 Asp Val Pro Pro Ser Tyr Ser His Tyr Tyr Ser Asn Pro Ser Tyr His Thr Leu Ser Gln Cys Ser Pro Asn Pro Pro Pro Asn Lys Val Pro Gly Pro Leu Phe Ala Ser Leu Gln Asn Pro Glu Arg Pro Gly Gly Ala Gln Gly His Asp Asn His Thr Thr Leu Pro Ala Asp Trp Lys His Arg 

Arg Glu Pro Pro Pro Gly Pro Leu Asp Arg Gly Ser Ser Arg Leu Asp 870 875 Arg Ser Tyr Ser Tyr Ser Tyr Ser Asn Gly Pro Gly Pro Phe Tyr Asp 885 890 Lys Gly Leu Ile Ser Glu Glu Glu Leu Gly Ala Ser Val Ala Ser Leu 900 905 910 Ser Ser Glu Asn Pro Tyr Ala Thr Ile Arg Asp Leu Pro Ser Leu Pro 915 920 925 Gly Gly Pro Arg Glu Ser Ser Tyr Met Glu Met Lys Gly Pro Pro Ser 935 940 Gly Ser Ala Pro Arg Gln Pro Pro Gln Phe Trp Asp Ser Gln Arg Arg 955 Arg Gln Pro Gln Pro Gln Arg Asp Ser Gly Thr Tyr Glu Gln Pro Ser 965 970 Pro Leu Ile His Asp Arg Asp Ser Val Gly Ser Gln Pro Pro Leu Pro 980 985 Pro Gly Leu Pro Pro Gly His Tyr Asp Ser Pro Lys Asn Ser His Ile 1005 995 1000 Pro Gly His Tyr Asp Leu Pro Pro Val Arg His Pro Pro Ser Pro Pro 1010 1015 1020 Leu Arg Arg Gln Asp Arg

<210> 114 <211> 747 <212> PRT <213> Homo sapiens

<400> 114 Leu Asn Pro Ser Asp Pro Asn Thr Cys Ser Phe Trp Glu Ser Phe Thr Thr Thr Lys Glu Ser His Ser Arg Pro Phe Ser Leu Leu Pro Ser 20 25 30 Glu Pro Cys Glu Arg Pro Trp Glu Gly Pro His Thr Cys Pro Ser Pro 40 45 Gln Thr Gln Arg Lys Leu Leu Ala Ser Arg Asp Ser Phe Cys Met Val 55 60 Cys Val Gly Ala Gly Val Gln Trp Arg Asp Arg Ser Ala Leu Gln Pro 65 70 75 Gln Thr Gly Asn Ala Leu Ser Met Arg Pro Gln Pro Arg Val Leu Ser 90 85 Gly Ala Pro Ser Leu Ala Ser Pro Gly His Thr Val Val Val Lys Thr 100 105 Asp His Arg Gln Arg Leu Gln Cys Cys His Gly Phe Tyr Glu Ser Arg 1.20 125 Gly Phe Cys Val Pro Leu Cys Ala Gln Glu Cys Val His Gly Arg Cys 135 Val Ala Pro Asn Gln Cys Gln Cys Val Pro Gly Trp Arg Gly Asp Asp 150 155 Cys Ser Ser Ala Pro Asn Cys Leu Gln Pro Cys Thr Pro Gly Tyr Tyr 165 170 Gly Pro Ala Cys Gln Phe Arg Cys Gln Cys His Gly Ala Pro Cys Asp 180 185 190 Pro Gln Thr Gly Ala Cys Phe Cys Pro Ala Glu Arg Thr Gly Pro Ser 195 200 205 Cys Asp Val Ser Cys Ser Gln Gly Thr Ser Gly Phe Phe Cys Pro Ser 215 220 Thr His Pro Cys Gln Asn Gly Gly Val Phe Gln Thr Pro Gln Gly Ser

المشكل المشكلة والمتحالية في أن المناطقة الفيالي في المناطقة التي المناطقة المناطقة المناطقة المناطقة المستعددين

Cys Ser Cys Pro Pro Gly Trp Met Gly Thr Ile Cys Ser Leu Pro Cys Pro Glu Gly Phe His Gly Pro Asn Cys Ser Gln Glu Cys Arg Cys His Asn Gly Gly Leu Cys Asp Arg Phe Thr Gly Gln Cys Arg Cys Ala Pro Gly Tyr Thr Gly Asp Arg Cys Arg Glu Glu Cys Pro Val Gly Arg Phe Gly Gln Asp Cys Ala Glu Thr Cys Asp Cys Ala Pro Asp Ala Arg Cys Phe Pro Ala Asn Gly Ala Cys Leu Cys Glu His Gly Phe Thr Gly Asp Arg Cys Thr Asp Arg Leu Cys Pro Asp Gly Phe Tyr Gly Leu Ser Cys Gln Ala Pro Cys Thr Cys Asp Arg Glu His Ser Leu Ser Cys His Pro Met Asn Gly Glu Cys Ser Cys Leu Pro Gly Trp Ala Gly Leu His Cys Asn Glu Ser Cys Pro Gln Asp Thr His Gly Pro Gly Cys Gln Glu His Cys Leu Cys Leu His Gly Gly Val Cys Gln Ala Thr Ser Gly Leu Cys Gln Cys Ala Pro Gly Tyr Thr Gly Pro His Cys Ala Ser Leu Cys Pro Pro Asp Thr Tyr Gly Val Asn Cys Ser Ala Arg Cys Ser Cys Glu Asn Ala Ile Ala Cys Ser Pro Ile Asp Gly Glu Cys Val Cys Lys Glu Gly Trp Gln Arg Gly Asn Cys Ser Val Pro Cys Pro Pro Gly Thr Trp Gly Phe Ser Cys Asn Ala Ser Cys Gln Cys Ala His Glu Ala Val Cys Ser Pro Gln Thr Gly Ala Cys Thr Cys Thr Pro Gly Trp His Gly Ala His Cys Gln Leu Pro Cys Pro Lys Gly Gln Phe Gly Glu Gly Cys Ala Ser Arg Cys Asp Cys Asp His Ser Asp Gly Cys Asp Pro Val His Gly Arg Cys Gln Cys Gln Ala Gly Trp Met Gly Ala Arg Cys His Leu Ser Cys Pro Glu Gly Leu Trp Gly Val Asn Cys Ser Asn Thr Cys Thr Cys Lys Asn Gly Gly Thr Cys Leu Pro Glu Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys Gln Arg Ser Cys Gln Pro Gly Arg Tyr Gly Lys Arg Cys Val Pro Cys Lys Cys Ala Asn His Ser Phe Cys His Pro Ser Asn Gly Thr Cys Tyr Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys Ser Gln Pro Cys Pro Pro Gly His Trp Gly Glu Asn Cys Ala Gln Thr Cys Gln Cys His His Gly Gly Thr Cys His Pro Gln Asp Gly Ser Cys Ile Cys Pro Leu Gly Trp Thr Gly His His Cys Leu Glu Gly Cys Pro Leu Gly Thr Phe Gly Ala Asn Cys Ser Gln Pro Cys Gln Cys Gly

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690
                      695
                                          700
Pro Gly Glu Lys Cys His Pro Glu Thr Gly Ala Cys Val Cys Pro Pro
           710
                                     715
Gly His Ser Gly Ala Pro Cys Arg Ile Gly Ile Gln Glu Pro Phe Thr
               725
                              730
Val Met Pro Thr Thr Pro Val Ala Tyr Asn Ser
           740
     <210> 115
     <211> 24
     <212> PRT
     <213> Homo sapiens
     <400> 115
Leu Gly Ala Val Ile Gly Ile Ala Val Leu Gly Ser Leu Val Val Ala
1
           5
                                  10
Leu Val Ala Leu Phe Ile Gly Tyr
           20
     <210> 116
     <211> 259
     <212> PRT
     <213> Homo sapiens
     <400> 116
Arg His Trp Gln Lys Gly Lys Glu His His His Leu Ala Val Ala Tyr
               5
Ser Ser Gly Arg Leu Asp Gly Ser Glu Tyr Val Met Pro Asp Val Pro
                             25
Pro Ser Tyr Ser His Tyr Tyr Ser Asn Pro Ser Tyr His Thr Leu Ser
       35
                         40
                                             45
Gln Cys Ser Pro Asn Pro Pro Pro Pro Asn Lys Val Pro Gly Pro Leu
                    55
                                        60
Phe Ala Ser Leu Gln Asn Pro Glu Arg Pro Gly Gly Ala Gln Gly His
65
                70
                                    75
Asp Asn His Thr Thr Leu Pro Ala Asp Trp Lys His Arg Arg Glu Pro
           85
                                 90
Pro Pro Gly Pro Leu Asp Arg Gly Ser Ser Arg Leu Asp Arg Ser Tyr
           100
                             105
Ser Tyr Ser Tyr Ser Asn Gly Pro Gly Pro Phe Tyr Asp Lys Gly Leu
       115
                          120
                                             125
Ile Ser Glu Glu Glu Leu Gly Ala Ser Val Ala Ser Leu Ser Ser Glu
                     135
                                        140
Asn Pro Tyr Ala Thr Ile Arg Asp Leu Pro Ser Leu Pro Gly Gly Pro
                150
                                     155
Arg Glu Ser Ser Tyr Met Glu Met Lys Gly Pro Pro Ser Gly Ser Ala
                           170
              165
                                                    175
Pro Arg Gln Pro Pro Gln Phe Trp Asp Ser Gln Arg Arg Arg Gln Pro
          180
                              185
                                                 190
Gln Pro Gln Arg Asp Ser Gly Thr Tyr Glu Gln Pro Ser Pro Leu Ile
                          200
    195
                                             205
His Asp Arg Asp Ser Val Gly Ser Gln Pro Pro Leu Pro Pro Gly Leu
  210
                     215
                                         220
Pro Pro Gly His Tyr Asp Ser Pro Lys Asn Ser His Ile Pro Gly His
225
                  230
                                      235
Tyr Asp Leu Pro Pro Val Arg His Pro Pro Ser Pro Pro Leu Arg Arg
                                  250
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Gln Asp Arg

<210> 117 <211> 497 <212> PRT <213> Mus msuculus

<400> 117 Ser Thr His Ala Ser Gly Asp Pro Val His Gly Gln Cys Arg Cys Gln . 5 10 Ala Gly Trp Met Gly Thr Arg Cys His Leu Pro Cys Pro Glu Gly Phe 20 25 Trp Gly Ala Asn Cys Ser Asn Thr Cys Thr Cys Lys Asn Gly Gly Thr 35 40 Cys Val Ser Glu Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly 55 Pro Ser Cys Gln Arg Pro Cys Pro Pro Gly Arg Tyr Gly Lys Arg Cys 70 75 Val Gln Cys Lys Cys Asn Asn Asn His Ser Ser Cys His Pro Ser Asp 85 90 Gly Thr Cys Ser Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys Ser Glu 100 105 110 Ala Cys Pro Pro Gly His Trp Gly Leu Lys Cys Ser Gln Leu Cys Gln 115 120 125 Cys His His Gly Gly Thr Cys His Pro Gln Asp Gly Ser Cys Ile Cys 130 135 140 Thr Pro Gly Trp Thr Gly Pro Asn Cys Leu Glu Gly Cys Pro Pro Arg 150 155 Met Phe Gly Val Asn Cys Ser Gln Leu Cys Gln Cys Asp Leu Gly Glu 165 170 Met Cys His Pro Glu Thr Gly Ala Cys Val Cys Pro Pro Gly His Ser 1.80 185 Gly Ala Asp Cys Lys Met Gly Ser Gln Glu Ser Phe Thr Ile Met Pro 200 Thr Ser Pro Val Thr His Asn Ser Leu Gly Ala Val Ile Gly Ile Ala 215 -220 Val Leu Gly Thr Leu Val Val Ala Leu Ile Ala Leu Phe Ile Gly Tyr 230 235 Arg Gln Trp Gln Lys Gly Lys Glu His Glu His Leu Ala Val Ala Tyr 245 250 Ser Thr Gly Arg Leu Asp Gly Ser Asp Tyr Val Met Pro Asp Val Ser 260 265 270 260 265 270 Pro Ser Tyr Ser His Tyr Tyr Ser Asn Pro Ser Tyr His Thr Leu Ser 275 280 285 280 Gln Cys Ser Pro Asn Pro Pro Pro Pro Asn Lys Val Pro Gly Ser Gln 290 295 300 Leu Phe Val Ser Ser Gln Ala Pro Glu Arg Pro Ser Arg Ala His Gly Arg Glu Asn His Thr Thr Leu Pro Ala Asp Trp Lys His Arg Arg Glu 325 330 335 Pro His Asp Arg Gly Ala Ser His Leu Asp Arg Ser Tyr Ser Cys Ser 340 345 350 Tyr Ser His Arg Asn Gly Pro Gly Pro Phe Cys His Lys Gly Pro Ile 355 360 365 Ser Glu Glu Gly Leu Gly Ala Ser Val Met Ser Leu Ser Ser Glu Asn 375 380 Pro Tyr Ala Thr Ile Arg Asp Leu Pro Ser Leu Pro Gly Glu Pro Arg 390 395

Glu Ser Gly Tyr Val Glu Met Lys Gly Pro Pro Ser Val Ser Pro Pro 405 410 Arg Gln Ser Leu His Leu Arg Asp Arg Gln Gln Arg Gln Leu Gln Pro 420 425 Gln Arg Asp Ser Gly Thr Tyr Glu Gln Pro Ser Pro Leu Ser His Asn 435 440 445 Glu Glu Ser Leu Gly Ser Thr Pro Pro Leu Pro Pro Gly Leu Pro Pro 455 450 460 Gly His Tyr Asp Ser Pro Lys Asn Ser His Ile Pro Gly His Tyr Asp 470 475 Leu Pro Pro Val Arg His Pro Pro Ser Pro Pro Ser Arg Arg Gln Asp 485 490 Arg

<210> 118 <211> 216 <212> PRT

<213> Mus musculus

<400> 118 Ser Thr His Ala Ser Gly Asp Pro Val His Gly Gln Cys Arg Cys Gln 10 Ala Gly Trp Met Gly Thr Arg Cys His Leu Pro Cys Pro Glu Gly Phe 25 Trp Gly Ala Asn Cys Ser Asn Thr Cys Thr Cys Lys Asn Gly Gly Thr 35 40 Cys Val Ser Glu Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly 55 Pro Ser Cys Gln Arg Pro Cys Pro Pro Gly Arg Tyr Gly Lys Arg Cys 70 75 Val Gln Cys Lys Cys Asn Asn Asn His Ser Ser Cys His Pro Ser Asp 90 85 Gly Thr Cys Ser Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys Ser Glu 100 105 110 Ala Cys Pro Pro Gly His Trp Gly Leu Lys Cys Ser Gln Leu Cys Gln 115 120 125 Cys His His Gly Gly Thr Cys His Pro Gln Asp Gly Ser Cys Ile Cys 135 140 Thr Pro Gly Trp Thr Gly Pro Asn Cys Leu Glu Gly Cys Pro Pro Arg 150 155 Met Phe Gly Val Asn Cys Ser Gln Leu Cys Gln Cys Asp Leu Gly Glu 1.65 170 Met Cys His Pro Glu Thr Gly Ala Cys Val Cys Pro Pro Gly His Ser 180 185 190 Gly Ala Asp Cys Lys Met Gly Ser Gln Glu Ser Phe Thr Ile Met Pro 195 200 Thr Ser Pro Val Thr His Asn Ser 210 215

<210> 119 <211> 24 <212> PRT

<213> Mus musculus

 $<\!400>$  119 Leu Gly Ala Val Ile Gly Ile Ala Val Leu Gly Thr Leu Val Val Ala l

Leu Ile Ala Leu Phe Ile Gly Tyr

<210> 120

<211> 257

<212> PRT

<213> Mus musculus

<400> 120

Arg Gln Trp Gln Lys Gly Lys Glu His Glu His Leu Ala Val Ala Tyr 10 Ser Thr Gly Arg Leu Asp Gly Ser Asp Tyr Val Met Pro Asp Val Ser 20 25 Pro Ser Tyr Ser His Tyr Tyr Ser Asn Pro Ser Tyr His Thr Leu Ser 35 40 Gln Cys Ser Pro Asn Pro Pro Pro Pro Asn Lys Val Pro Gly Ser Gln 55 60 Leu Phe Val Ser Ser Gln Ala Pro Glu Arg Pro Ser Arg Ala His Gly 75 Arg Glu Asn His Thr Thr Leu Pro Ala Asp Trp Lys His Arg Arg Glu 85 90 Pro His Asp Arg Gly Ala Ser His Leu Asp Arg Ser Tyr Ser Cys Ser 100 105 Tyr Ser His Arg Asn Gly Pro Gly Pro Phe Cys His Lys Gly Pro Ile 115 120 125 Ser Glu Glu Gly Leu Gly Ala Ser Val Met Ser Leu Ser Ser Glu Asn 135 140 Pro Tyr Ala Thr Ile Arg Asp Leu Pro Ser Leu Pro Gly Glu Pro Arg 150 1.55 Glu Ser Gly Tyr Val Glu Met Lys Gly Pro Pro Ser Val Ser Pro Pro 165 170 Arg Gln Ser Leu His Leu Arg Asp Arg Gln Gln Arg Gln Leu Gln Pro 180 185 Gln Arg Asp Ser Gly Thr Tyr Glu Gln Pro Ser Pro Leu Ser His Asn 195 200 Glu Glu Ser Leu Gly Ser Thr Pro Pro Leu Pro Pro Gly Leu Pro Pro 215 220 Gly His Tyr Asp Ser Pro Lys Asn Ser His Ile Pro Gly His Tyr Asp 230 235 Leu Pro Pro Val Arg His Pro Pro Ser Pro Pro Ser Arg Arg Gln Asp 245 250 Arg

<210> 121

<211> 636

<212> PRT

<213> Rattus sp.

<400> 121

Cys Asp Cys Ala Pro Gly Ala Arg Cys Phe Pro Ala Asn Gly Ala Cys Leu Cys Glu His Gly Phe Thr Gly Asp Arg Cys Thr Glu Arg Leu Cys Pro Asp Gly Arg Tyr Gly Leu Ser Cys Gln Asp Pro Cys Thr Cys Asp 100 105 110 Pro Glu His Ser Leu Ser Cys His Pro Met His Gly Glu Cys Ser Cys Gln Pro Gly Trp Ala Gly Leu His Cys Asn Glu Ser Cys Pro Gln Asp Thr His Gly Ala Gly Cys Gln Glu His Cys Leu Cys Leu His Gly Gly Val Cys Leu Ala Asp Ser Gly Leu Cys Arg Cys Ala Pro Gly Tyr Thr Gly Pro His Cys Ala Asn Leu Cys Pro Pro Asn Thr Tyr Gly Ile Asn 180 185 190 Cys Ser Ser His Cys Ser Cys Glu Asn Ala Ile Ala Cys Ser Pro Val Asp Gly Thr Cys Ile Cys Lys Glu Gly Trp Gln Arg Gly Asn Cys Ser Val Pro Cys Pro Pro Gly Thr Trp Gly Phe Ser Cys Asn Ala Ser Cys Gln Cys Ala His Glu Gly Val Cys Ser Pro Gln Thr Gly Ala Cys Thr Cys Thr Pro Gly Trp Arg Gly Val His Cys Gln Leu Pro Cys Pro Lys 260 265 270 Gly Gln Phe Gly Glu Gly Cys Ala Ser Val Cys Asp Cys Asp His Ser Asp Gly Cys Asp Pro Val His Gly His Cys Arg Cys Gln Ala Gly Trp Met Gly Thr Arg Cys His Leu Pro Cys Pro Glu Gly Phe Trp Gly Ala Asn Cys Ser Asn Ala Cys Thr Cys Lys Asn Gly Gly Thr Cys Val Pro Glu Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys Gln Arg Pro Cys Pro Pro Gly Arg Tyr Gly Lys Arg Cys Val Pro Cys Lys Cys Asn Asn His Ser Ser Cys His Pro Ser Asp Gly Thr Cys Ser Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys Ser Glu Ser Cys Pro Pro Gly His Trp Gly Leu Lys Cys Ser Gln Pro Cys Gln Cys His His Gly
405 410 415 Ala Thr Cys His Pro Gln Asp Gly Ser Cys Val Cys Ile Pro Gly Trp Thr Gly Pro Asn Cys Ser Glu Gly Cys Pro Ser Arg Met Phe Gly Val Asn Cys Ser Gln Leu Cys Gln Cys Asp Pro Gly Glu Met Cys His Pro Glu Thr Gly Ala Cys Val Cys Pro Pro Gly His Ser Gly Ala His Cys Lys Val Gly Ser Gln Glu Ser Phe Thr Ile Met Pro Thr Ser Pro Val Ile His Asn Ser Leu Gly Ala Val Ile Gly Ile Ala Val Leu Gly Thr 51.0 Leu Val Val Ala Leu Val Ala Leu Phe Ile Gly Tyr Arg His Trp Gln 

Lys Gly Lys Glu His Glu His Leu Ala Val Ala Tyr Ser Thr Gly Arg 535 Leu Asp Gly Ser Asp Tyr Val Met Pro Asp Val Ser Pro Ser Tyr Ser 545 550 555 His Tyr Tyr Ser Asn Pro Ser Tyr His Thr Leu Ser Gln Cys Ser Pro 570 565 Asn Pro Pro Pro Pro Asn Lys Ile Pro Gly Ser Gln Leu Phe Val Ser 580 585 Ser Gln Ala Ser Glu Arg Pro Asn Arg Asn His Gly Arg Asp Asn His 600 595 Ala Thr Leu Pro Ala Asp Trp Lys His Arg Arg Glu Ser His Asp Arg 615 Ala Phe Leu Arg His Gln Pro Pro Gly Pro Lys Val

<210> 122 <211> 500 <212> PRT <213> Rattus sp.

<400> 122 Met Gly Val Ile Cys Ser Leu Pro Cys Pro Glu Gly Phe His Gly Pro 10 Asn Cys Thr Gln Glu Cys Arg Cys His Asn Gly Gly Leu Cys Asp Arg 25 Phe Thr Gly Gln Cys His Cys Ala Pro Gly Tyr Ile Gly Asp Arg Cys
35 40 35 40 Arg Glu Glu Cys Pro Val Gly Arg Phe Gly Gln Asp Cys Ala Glu Thr 55 Cys Asp Cys Ala Pro Gly Ala Arg Cys Phe Pro Ala Asn Gly Ala Cys 70 75 Leu Cys Glu His Gly Phe Thr Gly Asp Arg Cys Thr Glu Arg Leu Cys 85 90 Pro Asp Gly Arg Tyr Gly Leu Ser Cys Gln Asp Pro Cys Thr Cys Asp 105 Pro Glu His Ser Leu Ser Cys His Pro Met His Gly Glu Cys Ser Cys 120 Gln Pro Gly Trp Ala Gly Leu His Cys Asn Glu Ser Cys Pro Gln Asp 135 Thr His Gly Ala Gly Cys Gln Glu His Cys Leu Cys Leu His Gly Gly 155 150 Val Cys Leu Ala Asp Ser Gly Leu Cys Arg Cys Ala Pro Gly Tyr Thr 165 170 175 Gly Pro His Cys Ala Asn Leu Cys Pro Pro Asn Thr Tyr Gly Ile Asn 180 185 190 Cys Ser Ser His Cys Ser Cys Glu Asn Ala Ile Ala Cys Ser Pro Val 195 200 Asp Gly Thr Cys Ile Cys Lys Glu Gly Trp Gln Arg Gly Asn Cys Ser 215 220 Val Pro Cys Pro Pro Gly Thr Trp Gly Phe Ser Cys Asn Ala Ser Cys 225 230 235 240 Gln Cys Ala His Glu Gly Val Cys Ser Pro Gln Thr Gly Ala Cys Thr 245 250 Cys Thr Pro Gly Trp Arg Gly Val His Cys Gln Leu Pro Cys Pro Lys 260 265 270 260 265 Gly Gln Phe Gly Glu Gly Cys Ala Ser Val Cys Asp Cys Asp His Ser 280 Asp Gly Cys Asp Pro Val His Gly His Cys Arg Cys Gln Ala Gly Trp

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290
                      295
Met Gly Thr Arg Cys His Leu Pro Cys Pro Glu Gly Phe Trp Gly Ala
                  310
                                     315
Asn Cys Ser Asn Ala Cys Thr Cys Lys Asn Gly Gly Thr Cys Val Pro
              325
                              330
Glu Asn Gly Asn Cys Val Cys Ala Pro Gly Phe Arg Gly Pro Ser Cys
           340
                           345
                                                350
Gln Arg Pro Cys Pro Pro Gly Arg Tyr Gly Lys Arg Cys Val Pro Cys
                                365
                          360
Lys Cys Asn Asn His Ser Ser Cys His Pro Ser Asp Gly Thr Cys Ser
                      375
                                        380
Cys Leu Ala Gly Trp Thr Gly Pro Asp Cys Ser Glu Ser Cys Pro Pro
                  390
                                     395
Gly His Trp Gly Leu Lys Cys Ser Gln Pro Cys Gln Cys His His Gly
              405
                                 410
Ala Thr Cys His Pro Gln Asp Gly Ser Cys Val Cys Ile Pro Gly Trp
          420
                             425
Thr Gly Pro Asn Cys Ser Glu Gly Cys Pro Ser Arg Met Phe Gly Val
      435
                         440
                                            445
Asn Cys Ser Gln Leu Cys Gln Cys Asp Pro Gly Glu Met Cys His Pro
                     455
                                        460
Glu Thr Gly Ala Cys Val Cys Pro Pro Gly His Ser Gly Ala His Cys
                470
                                     475
Lys Val Gly Ser Gln Glu Ser Phe Thr Ile Met Pro Thr Ser Pro Val
                                 490
Ile His Asn Ser
           500
     <210> 123
     <211> 24
     <212> PRT
     <213> Rattus sp.
     <400> 123
Leu Gly Ala Val Ile Gly Ile Ala Val Leu Gly Thr Leu Val Val Ala
            5
                                 10
Leu Val Ala Leu Phe Ile Gly Tyr
          20
     <210> 124
     <211> 112
     <212> PRT
     <213> Rattus sp.
     <400> 124
Arg His Trp Gln Lys Gly Lys Glu His Glu His Leu Ala Val Ala Tyr
1
               5
                                  10
Ser Thr Gly Arg Leu Asp Gly Ser Asp Tyr Val Met Pro Asp Val Ser
                             25
Pro Ser Tyr Ser His Tyr Tyr Ser Asn Pro Ser Tyr His Thr Leu Ser
       35
                         40
                                             45
Gln Cys Ser Pro Asn Pro Pro Pro Pro Asn Lys Ile Pro Gly Ser Gln
  50
                    55
                                        60
Leu Phe Val Ser Ser Gln Ala Ser Glu Arg Pro Asn Arg Asn His Gly
                  70
                                     75
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والمكل والأفرين المنافي والمنافعة والمنافي والمنطوعين والمتارين والمناوي والمارو والمتارين والمتارين

90

Arg Asp Asn His Ala Thr Leu Pro Ala Asp Trp Lys His Arg Arg Glu

Ser His Asp Arg Ala Phe Leu Arg His Gln Pro Pro Gly Pro Lys Val

85

105

110

<210> 125 <211> 28

<212> PRT <213> Homo sapiens

<400> 125

<210> 126 <211> 128 <212> PRT

<213> Homo sapiens

<400> 126

Lys Pro Lys Gly Met Thr Ser Ser Gln Trp Phe Lys Ile Gln His Met 10 Gln Pro Ser Pro Gln Ala Cys Asn Ser Ala Met Lys Asn Ile Asn Lys 20 25 30 His Thr Lys Arg Cys Lys Asp Leu Asn Thr Phe Leu His Glu Pro Phe 35 40 Ser Ser Val Ala Ala Thr Cys Gln Thr Pro Lys Ile Ala Cys Lys Asn 55 Gly Asp Lys Asn Cys His Gln Ser His Gly Pro Val Ser Leu Thr Met 70 75 Cys Lys Leu Thr Ser Gly Lys Tyr Pro Asn Cys Arg Tyr Lys Glu Lys 85 90 Arg Gln Asn Lys Ser Tyr Val Val Ala Cys Lys Pro Pro Gln Lys Lys 100 105 110 Asp Ser Gln Gln Phe His Leu Val Pro Val His Leu Asp Arg Val Leu 115 120 125

<210> 127 <211> 19 <212> PRT <213> Homo sapiens

 $<\!400\!>$  127 Met Pro Leu Leu Thr Leu Tyr Leu Leu Leu Phe Trp Leu Ser Gly Tyr 1 5 10 15 Ser Ile Ala

<210> 128 <211> 286 <212> PRT

<213> Homo sapiens

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35
                           40
Thr Ser Gly Ser Glu Gln Glu Val Lys Arg Asp Arg Val Ser Ile Lys
                       55
Asp Asn Gln Lys Asn Arg Thr Phe Thr Val Thr Met Glu Asp Leu Met
Lys Thr Asp Ala Asp Thr Tyr Trp Cys Gly Ile Glu Lys Thr Gly Asn
               85
                                 90
                                                  95
Asp Leu Gly Val Thr Val Gln Val Thr Ile Asp Pro Ala Ser Thr Pro
                              105
           100
                                                110
Ala Pro Thr Thr Pro Thr Ser Thr Thr Phe Thr Ala Pro Val Thr Gln
       115
                           120
                                              125
Glu Glu Thr Ser Ser Ser Pro Thr Leu Thr Gly His His Leu Asp Asn
  130
                      135
Arg His Lys Leu Leu Lys Leu Ser Val Leu Leu Pro Leu Ile Phe Thr
                150
                                     155
Ile Leu Leu Leu Leu Val Ala Ala Ser Leu Leu Ala Trp Arg Met
              165
                                  170
                                                     175
Met Lys Tyr Gln Gln Lys Ala Ala Gly Met Ser Pro Glu Gln Val Leu
          180
                             185
Gln Pro Leu Glu Gly Asp Leu Cys Tyr Ala Asp Leu Thr Leu Gln Leu
       195
                          200
                                           205
Ala Gly Thr Ser Pro Arg Lys Ala Thr Thr Lys Leu Ser Ser Ala Gln
                      215
Val Asp Gln Val Glu Val Glu Tyr Val Thr Met Ala Ser Leu Pro Lys
                 230
                                     235
Glu Asp Ile Ser Tyr Ala Ser Leu Thr Leu Gly Ala Glu Asp Gln Glu
               245
                                  250
Pro Thr Tyr Cys Asn Met Gly His Leu Ser Ser His Leu Pro Gly Arg
          260
                           265
Gly Pro Glu Glu Pro Thr Glu Tyr Ser Thr Ile Ser Arg Pro
                          280
     <210> 129
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<211> 150

<212> PRT

<213> Homo sapiens

<400> 129

Thr Gln Ile Thr Gly Pro Thr Thr Val Asn Gly Leu Glu Arg Gly Ser Leu Thr Val Gln Cys Val Tyr Arg Ser Gly Trp Glu Thr Tyr Leu Lys Trp Trp Cys Arg Gly Ala Ile Trp Arg Asp Cys Lys Ile Leu Val Lys Thr Ser Gly Ser Glu Gln Glu Val Lys Arg Asp Arg Val Ser Ile Lys Asp Asn Gln Lys Asn Arg Thr Phe Thr Val Thr Met Glu Asp Leu Met Lys Thr Asp Ala Asp Thr Tyr Trp Cys Gly Ile Glu Lys Thr Gly Asn Asp Leu Gly Val Thr Val Gln Val Thr Ile Asp Pro Ala Ser Thr Pro Ala Pro Thr Thr Pro Thr Ser Thr Thr Phe Thr Ala Pro Val Thr Gln Glu Glu Thr Ser Ser Ser Pro Thr Leu Thr Gly His His Leu Asp Asn Arg His Lys Leu Leu Lys

<210> 130 <211> 24 <212> PRT <213> Homo sapiens <400> 130 Leu Ser Val Leu Leu Pro Leu Ile Phe Thr Ile Leu Leu Leu Leu 1. 5 Val Ala Ala Ser Leu Leu Ala Trp 20 <210> 131 <211> 112 <212> PRT <213> Homo sapiens <400> 131 Arg Met Met Lys Tyr Gln Gln Lys Ala Ala Gly Met Ser Pro Glu Gln 1 10 Val Leu Gln Pro Leu Glu Gly Asp Leu Cys Tyr Ala Asp Leu Thr Leu 25 Gln Leu Ala Gly Thr Ser Pro Arg Lys Ala Thr Thr Lys Leu Ser Ser 40 Ala Gln Val Asp Gln Val Glu Val Glu Tyr Val Thr Met Ala Ser Leu 55 60 Pro Lys Glu Asp Ile Ser Tyr Ala Ser Leu Thr Leu Gly Ala Glu Asp 70 75 65 Gln Glu Pro Thr Tyr Cys Asn Met Gly His Leu Ser Ser His Leu Pro 90 85 Gly Arg Gly Pro Glu Glu Pro Thr Glu Tyr Ser Thr Ile Ser Arg Pro 105 100 <210> 132 <211> 21 <212> PRT <213> Homo sapiens <400> 132 Met Asp His Cys Gly Ala Leu Phe Leu Cys Leu Cys Leu Leu Thr Leu 5 10 Gln Asn Ala Thr Thr 20 <210> 133 <211> 507 <212> PRT <213> Homo sapiens <400> 133 Glu Thr Trp Glu Glu Leu Leu Ser Tyr Met Glu Asn Met Gln Val Ser 1 5 10 Arg Gly Arg Ser Ser Val Phe Ser Ser Arg Gln Leu His Gln Leu Glu 25 30 20 Gln Met Leu Leu Asn Thr Ser Phe Pro Gly Tyr Asn Leu Thr Leu Gln

45

60

40

55

Thr Pro Thr Ile Gln Ser Leu Ala Phe Lys Leu Ser Cys Asp Phe Ser

Gly Leu Ser Leu Thr Ser Ala Thr Leu Lys Arg Val Pro Gln Ala Gly

35

```
70
Gly Gln His Ala Arg Gly Gln His Ala Met Gln Phe Pro Ala Glu Leu
                                  90
Thr Arg Asp Ala Cys Lys Thr Arg Pro Arg Glu Leu Arg Leu Ile Cys
          100
                             105
Ile Tyr Phe Ser Asn Thr His Phe Phe Lys Asp Glu Asn Asn Ser Ser
     115
                         120
                                            125
Leu Leu Asn Asn Tyr Val Leu Gly Ala Gln Leu Ser His Gly His Val
                      135
                                         140
Asn Asn Leu Arg Asp Pro Val Asn Ile Ser Phe Trp His Asn Gln Ser
                 150
                                      155
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Leu Asn Ile Ala Phe Leu Leu Ser Pro Ala Phe Ala Met Ser Pro Val
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Pro Gly Ser Ala Cys Thr Ala Leu Ala Ala Leu His Tyr Ala Leu
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Leu Leu Gly Arg Val Tyr Asn Ile Tyr Ile Arg Arg Tyr Val Phe Lys
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His Asp Thr Val Thr Val Leu Gly Leu Thr Val Leu Leu Gly Thr Thr
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Trp Ala Leu Ala Phe Phe Ser Phe Gly Val Phe Leu Leu Pro Gln Leu
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Form PCT/ISA/\$10 (second sheet) (July 1998)&

	PCT/US00/18198
Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)	
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:	
2. Claims Nos.: because they relate to parts of the international application that do not comply van extent that no meaningful international search can be carried out, specific	
Claims Nos.:     because they are dependent claims and are not drafted in accordance with the sec	cond and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)	
This International Searching Authority found multiple inventions in this international application, as follows:	
Please See Extra Sheet.	
As all required additional search fees were timely paid by the applicant, this into claims.	ernational search report covers all searchable
<ol> <li>As all searchable claims could be searched without effort justifying an addition of any additional fee.</li> </ol>	nal fee, this Authority did not invite payment
3. As only some of the required additional search fees were timely paid by the appronly those claims for which fees were paid, specifically claims Nos.:	plicant, this international scarch report covers
4. X No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-10 and 12	
Remark on Protest The additional search fees were accompanied by the	ne applicant's protest.
No protest accompanied the payment of additional	search fees.

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1998)\*

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1-10 and 12, in so far as they are drawn to Intercept 340, polynucleotides of SEQ ID NOS: 1 and 3, vector, host cell, method of producing a protein recombinantly and protein of SEQ ID NO: 2.

Groups II-VII, claim(a) 1-10 and 12, in so far as they are drawn to the next six polynucleotides of distinct cDNA clones and encoded proteins, identified as Mango 003, Mango 347, Tango 272, Tango 295, Tango 354 and Tango 378, as listed in Tables 1 and 2.

Groups VIII-XIV, claim(s) 11 and 15, in so far as they are drawn to antibodies to one of the seven proteins listed above.

Groups XV-XXI, claims 13, 14, 19, 20 and 22, in so far as they are drawn to a method for detecting the presence of in a sample or identifying a compound which binds to or modulates the activity of a polypeptide of one of the seven proteins listed above.

Groups XXII-XXVII, claims 16 and 17, in so far as they are drawn to a method for detecting the nucleic acids of one of the seven cDNA clones listed above.

Groups XXIX-XXXV, claim 18, in so far as it is drawn to a kit comprising a compound of unspecified constitution which selectively binds to a nucleic acid molecule of the seven cDNA clones listed above.

Groups XXXVI-XLII, claim 21, in so far as it is drawn to a method for modulating the activity of one of the seven proteins listed above.

The inventions listed as Groups I-XLII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Group I corresponds to the first invention wherein the first product is the polynucleotide and the first method of using is the method of making the protein. Note that there is no method of making the polynucleotide. The invention also includes the protein made. Each of groups II-VII does not share the same or corresponding special technical feature because each group is drawn to a different polynucleotide and encoded protein, and each of groups VIII-XLII does not share the same or corresponding special technical feature because each group is drawn to different compounds or methods of using the seven polynucleotides and encoded proteins. This Authority therefore considers that the several inventions do not share a special technical feature within the meaning of PCT Rule 13.2 and thus do not relate to a single general inventive concept within the meaning of PCT Rule 13.1.